Cost-effectiveness of screening programme for abdominal aortic aneurysm

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Master thesis

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FOREWORD

Abdominal aortic aneurysm is a major cause of morbidity and mortality among men in the Western countries, particularly in men older than 65 years. In most cases the aneurysm is asymptomatic, and remains undetected until rupture. The mortality rate of a ruptured aneurysm is high. The overall mortality from AAA can be reduced by early detection through screening programmes and elective repair. Ultrasound is considered practical for screening. The method is available, but the cost-effectiveness in Norway is unknown.

I would like to thank my supervisor, Ivar Sønbø Kristiansen (MD PhD MPH, at The Institute of Health Management and Health Economics, University of Oslo) for his constant enthusiastic approach and pure desire to assist when needed. His supervision in terms of professional advice regarding the thesis has been very helpful. Nevertheless, he has helped me to reach out to other with valuable contacts such as my co-supervisor Jørgen J. Jørgensen (Chief surgeon at Aker University Hospital) and Torbjørn F. Wisløff (Statistician at The Institute of Health Management and Health Economics, University of Oslo. I would like to acknowledge Jørgensen for providing valuable information on the cost data and for supervising on the pathogenesis, treatment, and diagnosis of the disease, and Wisløff for helping me out of multiple challenges with the model.

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ABBREVIATIONS AND ACRONYMS

AAA	Abdominal aortic aneurysm
CBA	Cost-benefit analysis
CEA	Cost-effectiveness analysis
CUA	Cost-utility analysis
CT	Computed tomography
EVAR	Endovascular repair
GP	General practitioner
ICER	Incremental cost-effectiveness ratio
LYG	Life-years gained
NOK	Norske Kroner
OR	Open repair
PPV	Positive predictive value
US	Ultrasonography
WHO	World Health Organization

ABSTRACT

Background: Abdominal aortic aneurysm is the 10th leading cause of death representing 1.3% of all fatalities among men aged 65-85 in the Western countries. Screening procedures are available, but the cost-effectiveness for Norway is unknown.

Objective: To predict the costs and impact on life expectancy of an AAA screening program.

Methods: A Markov model was developed to compare the effect of a single ultrasound screening for a cohort of men at the age 65 with the current no screening strategy. The following health states were included: AAA≤30 mm, AAA30–39 mm, AAA40–54 mm, AAA55-59 mm, AAA≥60 mm with risk factors, AAA>60 mm with unknown risk factors, Inoperable AAA55-59 mm, Inoperable AAA≥60 mm , Post EVAR (patients who survive endovascular repair will transit to this health state after repair), Dead from aneurysm and Dead from other causes. Transition probabilities were derived from the medical literature and the cycle length was one year. Incremental cost per life year gained was calculated and sensitivity analysis and discounting of future effects were performed.

Outcome measures: The results are expressed as incremental costs, incremental life years gained and cost per life year gained.

Results: The average life time AAA-related cost of a 65-year-old patient in the non-screening group was NOK3010 (NOK2032 discounted) and in the screening group NOK6074 (NOK4686 discounted), resulting in incremental costs of NOK2654 per screened patient. The life expectancy was 16.3832 (11.7051 discounted) for non-screened patients and 16.4351 (11.7345 discounted) for screened, or a life year gained of 0.0294. The cost per life year gained was NOK90300.

The results of the one-way sensitivity analyses indicate that the conclusion is not threatened by any realistic change of the model input.

Interpretation/conclusion: One-time ultrasonography screening for AAA men at the age 65 appears to be cost-effective.

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1. INTRODUCTION

Abdominal aortic aneurysm (AAA) is a common condition that affects approximately 2-9% of men and 1-2% of women. AAA is the 10th leading cause of death (1.3%) among men aged 65-85 in the Western countries. The aneurysms are typically asymptomatic, but the aneurysm may evolve and eventually rupture. A rupture of aneurysm is associated with high mortality and most patients die before they come to surgery. These deaths can be prevented by early detection through screening programmes and elective repair.

This thesis will start by describing abdominal aortic aneurysm and its pathogenesis in chapter 1. In chapter 2, it will describe the epidemiology of the disorder, while Chapter 3 and 4 explore various diagnostic and therapeutic strategies. Chapter 5 explains the basic concepts of economic evaluation, and in chapter 6 the research question is explicitly defined. The methods are described in chapter 7, including some basic theory of Markov modelling, a description of the structure of the model and an overview of the literature search. Finally, the results and discussion are presented in chapters 8 and 9.

1.1 Aortic aneurysm

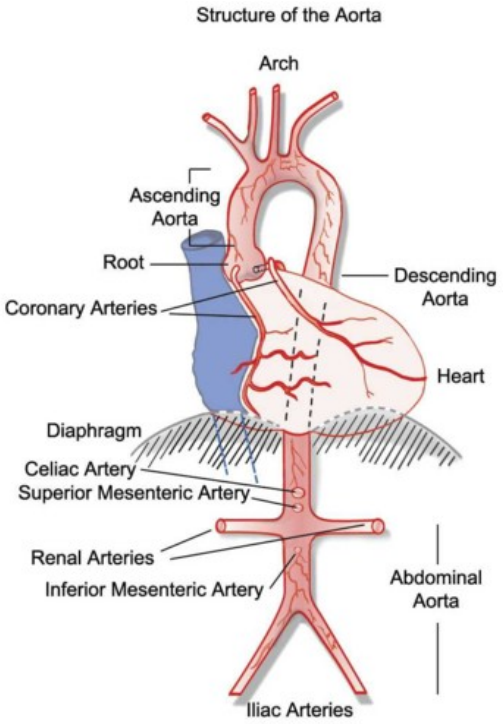
"An aneurysm is defined as a focal dilation of the aorta involving an increase in diameter of at least 50 percent as compared to the expected normal diameter" (Ernst 1993). An aortic aneurysm is a general term for any abnormal expansion of the aorta, caused by a weakening in an artery wall as blood is pumped through it. The weakening of the artery wall is most frequently a result of atherosclerosis, while other causes will also be explained later in this thesis.

1.2 Anatomy and physiology of aorta

Aorta is the main artery of the body and plays a key role in the cardiovascular system. It arises from the left ventricle of the heart and carries blood out to all organs in the body. In addition to aorta, there are also various other types of vessels in the cardiovascular system: arteries (aorta and branches of the aorta), arterioles, capillaries, venules and veins. All blood vessels have the same basic structure with three layers of wall: one interior layer (tunica intima), one middle layer (tunica media), and one outer layer (tunica externa). Tunica intima consists of a layer of endothelial cells and a thin layer of connective tissue. Tunica media consists of varying amount of vascular smooth muscle, while tunica externa is entirely made of connective tissue. A normal aortic diameter is approximately 17-21 mm (infrarenal) for men and 15-19 mm (infrarenal) for women and the wall of the aorta is 1,5 mm thick, but the dimension will depend on various factors such as sex, age and blood pressure (Bjålie, Haug, & Sjaastad 2000;Moore 2006).

Aorta is divided into three different parts: aorta ascendens, arcus aortae and aorta descendens. Aorta ascendens is the part which departs from the left ventricle and is ascending to the arcus aortae. Arcus aortae cross to aorta descendens, which pass downward along the vertebral column and through the diaphragm. Aorta thoracalis is the area of aorta above diaphragm, while aorta below diaphragm is named abdominal aorta (aorta abdominalis) (Bjålie, Haug, & Sjaastad 2000).

Figure 1: Structure of the Aorta



1.3 Atherosclerosis

Atherosclerosis is the most frequent type of arteriosclerosis, which means dense arteries (Næss 2002). Atherosclerosis is characterized with congestion of lipids, particularly cholesterol in the intima of the artery. The lipids are absorbed by macrophages[21], but will also stay outside the macrophages and create crystals of cholesterol**.** The macrophages secrete growth factors, which induce the plain muscle cells in the area to divide. The alteration can be seen as yellow plaques. The process

[21] A type of white blood cells that ingests foreign material.

may be reversible, but generally it evolves. Progressively, the plaques will elevate, as a form of a cushion, above the surface of intima. The lipids, within and outside the macrophages, will irritate the artery wall and cause inflammation. Gradually, it will develop a bulge which will narrow the lumen of the artery and create stenosis. Occasionally, the plaque below intima will rupture and develop into an ulcer (plaque rupture). As the atherosclerosis process progresses, the alteration will also occur in the media and the entire artery wall will be weakened (Næss 2002). The atherosclerosis process may eventually cause thrombosis in the arteries. A thrombosis does often cause a block in the blood stream and infarction. Thrombosis in the legs blocks the blood from flowing back to the heart and causes a congestion of blood which cause swelling of the legs and severe pain. If the thrombosis occurs in the heart or in the brain it may lead to infarction of the heart or cerebral infarction. Thrombosis may also occur in the aorta, but because of the size dimension of the aorta, it will not cause a complete block in the blood stream but is identified as a focal dilation of the artery, called aneurysm. Aneurysms are round (saccular) or more often tube like (fusiform) and the latter is most frequent.

The stretched vessels may be symptom free, but may also cause discomfort as abdominal and back pain. Additionally, compression of nerve roots can cause leg pain of numbness. Untreated aneurysms will become progressively larger. As the aneurysms evolve, the risk for rupture increases. A rupture causes severe pain, massive internal hemorrhage, and death within minutes or hours unless the patient has successful surgery. The risk of rupture depends on the size. The risk is large once the aneurysm has reached approximately 5 cm, but some may also swell to over 15 cm before they rupture (Krohg-Sørensen 2001).

1.3.1 Risk factors

From epidemiological screening studies, risk factors for atherosclerosis and AAA have been identified. Smoking is probably one of the most important environmental risk factors (Sakalihasan, Limet, & Defawe 2005). Case control studies report that

there is significant clinical association between smoking and the presence of AAA. Genetic factors do also seem to have important effects. Kuivaniemi and co-workers report that the disorder is present 15-19% in the first-degree relatives, but the frequency is only 1-3% in unrelated patients (Kuivaniemi et al. 2003).

Other risk factors are hypertension, hyperlipdaemia, coronary artery disease, history of lower extremity bypass operation, claudication, ischemic rest pain and carotid artery disease, trauma, elevated cholesterol level and overweight (Berkow, Fletcher, & Beers 1997;Lee et al. 2002).

Aortic aneurism has traditionally been regarded as a consequence of atherosclerosis. However, this conventional view has been challenged in recent years. Firstly, aneurysms have been associated with inflammation in the vessel wall or injuries in intima or media. Marfans syndrome is a disease which attacks the connective tissue. The disease is a congenital weakness in the vessel walls which cause the aneurysm. The weakening of the layer of the aortic wall can also be a consequence of inflammatory diseases such as syphilis and tuberculosis. However, such cases are rare in Norway because of the low prevalence of those diseases.

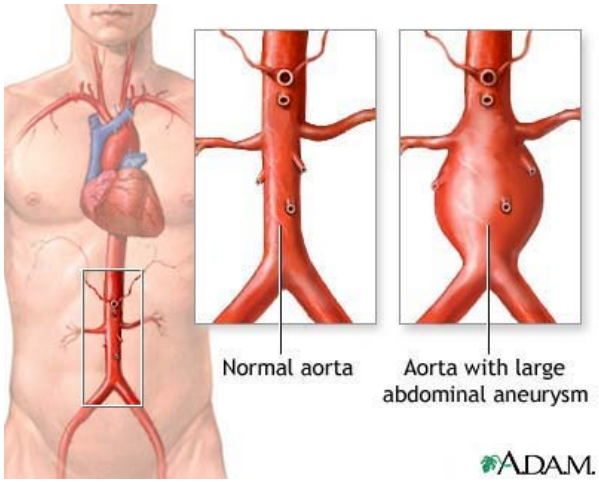
The aneurysms increase exponentially and the risk of rupture increases with size.

1.3.2 Classification of aneurysms

Aortic aneurysm is classified according to the anatomic location. Aortic root aneurysm appears on the aortic root (the sinuses of Valsalva), while the thoracic aorta aneurysms are found on the thoracic aorta. The most common form of aortic aneurysm is abdominal aortic aneurysm (AAA). Three quarters of all aneurysms develop in this segment, which runs from the diagphram to the lower abdomen, where aorta divides into two iliac arteries. One may also experience aortic aneurysms which involve both the thoracic and abdominal aorta (thoracabdominal aortic aneurysm). One reason that AAA is more common than thoracic aorta, is that content elastin is lower in the abdominal aorta. Elastin is an important load-bearing protein in connective tissue and is found in the wall of aorta (Næss 2002). Its elastic property

allows many tissues in the body to resume their shape after stretching or contracting. Another explanation of higher frequency of AAA than other types of aneurysm is that the abdominal aorta does not possess blood vessels, and repair is therefore hindered (van der Vliet & Boll 1997).

Figure 2: Illustration of aorta with large abdominal aneurysm



2. EPIDEMIOLOGY

Abdominal aorta aneurysm occurs mostly among men older than 65 years, and has been claimed to cause 1.3% of all deaths among men in the age of 65-85 in developed countries(Lundholm J. et al. 1999;Sakalihasan, Limet, & Defawe 2005). Statistics Norway report that 301 men aged 65 and older died from AAA (or similar diseases in the same category) in 2005 (Statistics Norway 2005c). At the same time, the number of deaths among women were only 177(Statistics Norway 2005a). Although AAA is estimated to be the tenth most common cause of mortality, the estimates of mortality may be hampered by low rates of post mortems. Sudden ruptures are likely to be certified as cardiac death in the absence of autopsy, when AAA was not documented ante mortem and may affect the reported number of deaths (Bergqvist, Bjorck, & Wanhainen 2008).

2.1 Incidence of Abdominal aortic aneurysm

The incidence of AAA is by some argued to have increased during the past two decades. Zankl and co-workers point out the importance of a widespread surveillance of AAA. In recent years, an increasing number of mostly asymptomatic patients have been detected during routine abdominal screening and may contribute to an increase in the incidence (Zankl et al. 2007). Sakalihasasn and co-workers argue that due to the ageing of the population, the rise in the number of smokers, and improved diagnostic tools, the reported incidence of abdominal aorta aneurism has increased (Sakalihasan, Limet, & Defawe 2005). This is in contrast with trends seen in stroke and coronary heart disease (Norman et al. 2004). Hence, it is difficult to predict any specific numbers on the incidence. However, one does know that the incidence increases with age and as the disorder is categorized as a “lifestyle disease”, the incidence will to some extent be reflected by the lifestyle of the population (Sakalihasan, Limet, & Defawe 2005).

One difficulty with investigating the incidence is that one needs to make a repetitive measurement of the probabilities. This is both time and cost consuming. In order to measure the number of new cases of AAA, one also needs to screen the target group before they develop the disease. In real life it is difficult to predict who these persons will be.

2.2 Prevalence of Abdominal aortic aneurysm

Few epidemiological studies of AAA have been done in Norway in recent years. However, a population-based study in Tromsø in Norway found that an aneurysm was present in 2.2 % of the women and 8.9 % of the men (Singh et al. 2001). The study reports age and sex specific prevalence rates. For men aged 55-64, 65-74 and 75-84 the percentage of subjects with AAA were 6.2, 14.1 and 19.8 respectively. For the same age groups the percentage of women with AAA was 0.7, 4.2 and 5.2 respectively. The prevalence of AAA is higher among men than women. From the Tromsø study the prevalence is estimated to be four times higher among men than women (Singh, Bonaa, Jacobsen, Bjork, & Solberg 2001). This is also supported by similar international studies (Lederle, Johnson, & Wilson 2001).

The prevalence numbers from Norway are somewhat higher compared to other countries. International prevalence rates are estimated between 1.0-2.2 for women and 1.3-8.9% for men (Zankl, Schumacher, Krumsdorf, Katus, Jahn, & Tiefenbacher 2007). As we have few epidemiological studies on AAA in Norway, we do not know if the variation is due to the design of the study or a matter of epidemiological and demographic differences between the countries.

3. DIAGNOSIS

About half of the deaths that are attributed to rupture take place before the patient reaches the hospital (Ashton et al. 2002;Silverstein et al. 2005). Among those who reach the hospital alive, less than half survive the emergency repair (Ashton, Buxton, Day, Kim, Marteau, Scott, Thompson, & Walker 2002;Lundholm J., Hatlinghus S., Wirsching J, Amundsen S., Staxrud L.E., Gjølberg T., Hafsahl G., Oskarsson W., Krohg-Sørensen, Brekke M., & Myhre H.O. 1999). Elective repair is reported to be more successful than emergency repair, and hence the purpose of treatment is to detect the aneurysm before it ruptures (Ashton, Buxton, Day, Kim, Marteau, Scott, Thompson, & Walker 2002). The aneurysms is mainly detected during routine physical examination (palpation of abdomen) or found incidentally through routine medical tests, when evaluating other diseases such as lung diseases.

Abdominal palpation is the original method to detect AAA (Lederle & Simel 1999). Palpation is the use of doctor's hands to detect alteration in the size of the organs. Palpation has low costs, as no further equipment is required. However, the accuracy is often limited by patient obesity and the sensitivity and specificity will vary with the experience of the doctor (Lynch 2008). Furthermore, the sensitivity rate increases with the size of the aneurysm and presence of any recognisable risk factors and characteristics of the patient. One single report indicates that the physical examination has a sensitivity rate which ranged from 33% to 100%, while the specificity ranged from 75% to 100% (Lynch 2008). Palpation, as diagnostic tool, results therefore in a large proportion of false-negative and false-positive findings and a consequent poor positive predictive value (PPV).[22] In the same report the PPV ranged from 14% to 100%

Maximal aneurysm diameter is the often considered as the best predictor of rupture and the decision on repair is mainly based on this measurement (Sprouse et al. 2003).

[22] PPV measures the proportion of patients with positive test results who are correctly

A size difference of only few millimeters determines whether or not a patient is offered surgery. Hence, the sensitivity and specificity is of great importance. The principal modalities used to measure AAAs are ultrasonography (US) and computed tomography (CT) (Sprouse, Meier, III, Lesar, DeMasi, Sood, Parent, Marcinzyck, & Gayle 2003). Both methods reproduce measurements which are within an adequate range.

3.1 Ultrasonography

Abdominal ultrasonography is an ultrasound-based diagnostic imaging technique used to examine the interior of the abdomen. The technique involves exposing part of the body to high-frequency sound waves to produce pictures of the inside of the body. Unlike x-ray, the individual is not exposed to ionizing and the method is painless and supposedly safe.

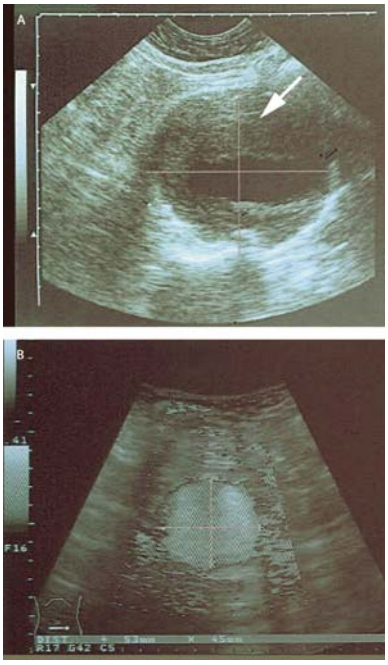
The sensitivity and specificity of ultrasonography are both close to 100% when compared with operative findings (Silverstein, Pitts, Chaikof, & Ballard 2005). Still, in some cases, the aorta can not be visualized due to bowel gas, obesity or periaortic disease (Ernst 1993;Silverstein, Pitts, Chaikof, & Ballard 2005). The technique is often imprecise in measuring the size of the aneurysm. The size is important for prognostic reasons, but is also essential in determining the growth rate of the aneurysm.

Interobserver variability in measurements obtained by ultrasonography is reported to range from 0.22 to 1.55 cm (Knaut et al. 2005). Singh and co-workers indicate that both the intra- and inter-observer variability were less than 4 mm in measurements of

aximal infrarenal[23] aortic diameter. However, the inter-and intra-observer variability[24] will vary with experience among sonographers (Singh et al. 1998).

Ultrasonography provides structural detail of vessel walls and atherosclerotic plaque. Its advantage is that it is easily available and transportable, and is absent of significant side effects.

Figure 3: Ultrasonography images of an infrarenal aortic aneurysm



3.2 Computed tomography

Unlike ultrasonography, computed tomography (CT) uses x-rays (ionising radiation) to create cross sectional images of the abdominal area. The individual will be asked to lie down so that the small detectors inside the CT scanner, can measure the amount of x-rays that make it through the abdomen. The information from detectors

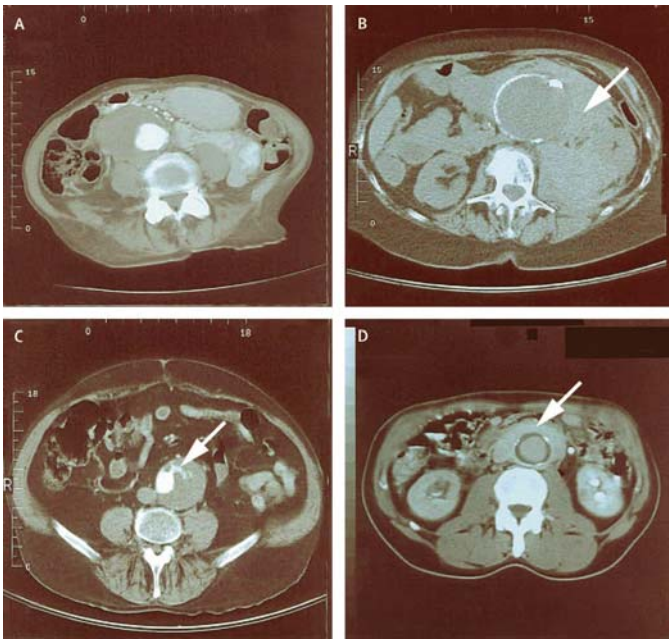
[23] Infrarenal means located below the kidneys.

[24] Interobserver variability is defined as the degree of divergence between two or more observers, while intraobserver variability is defines as the degree of divergence within one observer.

undergoes sophisticated computer analyses that allow the creation of several individual images, which are called slices.

Computed tomography is also recognized with sensitivity and specificity close to 100% compared to operative findings (Silverstein, Pitts, Chaikof, & Ballard 2005). Several authors have noted a difference between AAA measurements obtained with ultrasonography and CT. CT is more accurate in estimating the aneurysm size than ultrasonography and considered as the gold standard, although evidence is lacking (Silverstein, Pitts, Chaikof, & Ballard 2005;Singh et al. 2004). The reproducibility rate of CT is also reported to be somewhat higher than for ultrasonography. Knaut and co-workers report that the inter-observer variability obtained by CT range from 0.28 to 0.70 cm (Knaut, Kendall, Patten, & Ray 2005). Singh and co-workers report that the absolute intra-observer difference of the maximal infrarenal aortic diameter was 2 mm or less in 94% of intra-observer pairs (Singh et al. 2003).

Figure 4: Computed tomography images of abdominal aortic aneurysm



Variability is caused by differences in observer expertise, time of testing, method of measurement and the definition of the measurement size (Singh, Jacobsen, Solberg,

Kumar, & Arnesen 2004). Moreover, a precise correlation between CT and ultrasonography is difficult because of the real time variation in the aortic diameter, due to differences in the pulsatile flow phases through the vessel.

Generally, ultrasound tends to slightly underestimate the aortic diameter, although this phenomenon is taken into consideration in the literature. Ultrasound is considered practical for screening, whereas CT is the preferred method for preoperative imaging in patients with AAAs (Vidakovic et al. 2007). I will go further into the methods used in my model in chapter 7.

Although, it is reported that both ultrasound and CT have specificity and sensitivity close to 100%, it should be noted that the specificity and sensitivity only concerns the size of the aneurysm. Both devices do not have the same level of specificity and sensitivity, when it comes to predict which of the detected aneurysm that will rupture and cause death. These issues may be important when considering whether or not to implement a screening program for AAA. Further considerations are also discussed in the following chapter.

3.3 Screening and ethics

The World Health organization (WHO) has defined screening as “a medical investigation which does not arise from a patient’s request for advice for specific symptoms or complaints”(Wilson & Jungner 1968).

In contrast to traditional medical practice, in which the patient asks the doctor for advice and treatment, the contact is now initiated by the health care providers. Regardless of which part that initiated the contact, the doctors need to assume the same duty of care and that the patients must hold the same understanding of what the treatment involves. Hence, certain criteria are required for a screening process to be undertaken. WHO has suggested the following criteria:

1. The disease should be an important health problem
2. A generally acceptable method of treatment must be available

3. The policy of treatment must be clear
4. Provision for diagnosis and treatment must be available
5. The disease must have a detectable latent stage
6. A suitable screening method must be available
7. The screening method must be accepted by the target population
8. The natural course of the disease must be known.
9. The program must be cost-effective
10. The treatment of the disease should favour the prognosis of the patients

These criteria will be comprehensively evaluated later in this thesis, when discussing the results from the analysis. However, the essence of the criteria is that disease needs to be sufficiently important, and that the outcome of the treatment at the presymptomatic stage benefits the patient. In other words; the purpose of screening is to identify the disease or risk factor in its preclinical stage, in order to improve morbidity and mortality and to gain a long term benefit in terms of avoided treatment in the future. The benefit can also involve reduced costs. In recent years, reducing health expenditures has been on the top agenda, and screening may be seen as one strategy in fighting this challenge. Treatment at an early stage may not only have positive effects on the patient's health, but may also be cost-saving.

Unfortunately, screening does not always live up to the expectations in the previous paragraph, as screening also involves "psychological costs". There are particular three aspects which cause these "psychological costs"; patients do not understand precisely what the test is for, they are not acquainted with the accuracy of the test and they are not familiar with what the test results imply (Marteau 1990). Patients, who receive an invitation to a screening programme, may experience induced anxiety in the sense that an invitation make people feel ill when they really are healthy. Furthermore, the patients should know what the sensitivity and specificity rates of the test are, and warned that a test can never produce perfect results (Edward & Hall 1992). Induced anxiety can also be experienced both for false positive and false negative results. Because there is a trade off between false reassurance and false alarms, this does not mean that each patient will benefit from screening (Mant &

Fowler 1990). In the case of a positive result one need to make sure that the patient is explained the consequences of such a result. For most patients a positive result will involve either surveillance or elective repair. However, some patients will also be considered as unfit for repair, because their aneurysm is less than the defined threshold for repair, and some are also inoperable due to risk factors. These patients need to continue on living knowing that they have a "time bomb" in their stomach. The "psychological costs" of the screening program for these patients are not to be neglected. The "time bomb" may go off at any time and without notice, and the only way to control them perfectly is serial measurements. Patients who have a detected aneurysm will, however, have ultrasound examination only four times to once a year. For a patient who thought he was perfectly well and then is left with the knowledge that he has a life threatening disease, the surveillance program may not be experienced as comprehensive and adequate (Brearly S. & Johnson J.N 2008). Furthermore, patients must be familiar with that an attendance in a screening program also involves several follow-ups. If the patient does not have this information, it may lead to induced anxiety when they receive additional invitations. In general one need to weight the effect of the patients who get their aneurysm detected and benefit from elective against the effect of those who are considered as unfit for repair.

Another ethical issue of screening is the phenomena often referred to as medicalization. Medicalization means, literary, "to make medical", but in practical manner the concept also has a wider meaning. In recent years, concepts of health and disease have extended their meaning to involve a broader aspect of people's life and the medical field of responsibility. This field of responsibility involves both knowledge and tasks, and includes the right to define what should be considered as a disease (Lian Olaug S. 2006). Medicalization can also be looked upon as the process which causes an extensive use of medical expertise and terminology. As a result of the phenomena a larger part of people's life can be defined as relevant for medical intervention and become part of the area of responsibility of the health care sector. This may not only be problematic for ethical reasons, but may also cause excessive health expenses.

In order to achieve an effective screening program it is important that the staff is sufficiently trained, that there exists protocols for positive results and a united agreement on how the patients should be managed.

4. TREATMENT

Treatment for an aortic aneurysm will depend on the size and location of the aneurysm, as well as the person's general health, including age and risk. Treatment options include surveillance and surgery.

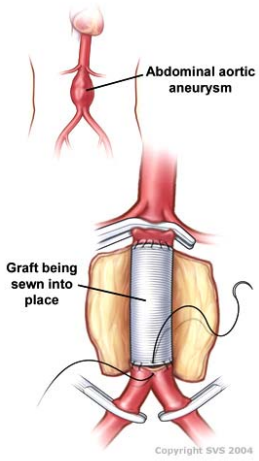
Surveillance is considered as the appropriate option for patients with small aneurysms. The classification of aneurysms varies, but in Norway one monitors patients until they reach the size of approximately 55 mm (Lundholm J., Hatlinghus S., Wirsching J, Amundsen S., Staxrud L.E., Gjølberg T., Hafsahl G., Oskarsson W., Krohg-Sørensen, Brekke M., & Myhre H.O. 1999;Statistics Norway 2005c). This kind of treatments is sometimes referred to as “watching-and-waiting”, as the patient is monitored through ultrasound or CT once or more a year. Surgery is the recommended treatment strategy for patients with aneurysms larger than 55 mm and for those with rapidly increasing aneurysm (Brown P.T.MD, David T.Zelt MD, & Boris Sobolev PhD 2003). There are mainly two approaches to treat abdominal aortic aneurysm; open abdominal surgery and endovascular surgery.

4.1 Open abdominal surgery

Open abdominal surgery is the conventional surgery strategy for AAA (Bosch et al. 2002;Scott et al. 1995).The procedure involves that the vascular surgeon makes a large cut in the abdominal wall to identify the aorta at the site of the aneurysm and clamps the aorta to keep it from bleeding. The surgeon now replaces the weakened area with a graft, which is sewn in place with permanent suture material. The graft is artificial (dacron or goretex) and will replace the aorta and secure the arterial circulation to the pelvic and the lower extremities (Medline Plus Encyclopedia 2008).

The length and risk of the surgery will depend on the extent of the aneurysm and the patient’s health. Most patients stay in the hospital for one week and the recovery time is usually one month to six weeks.

Figure 5: Illustration of open repair stent graft

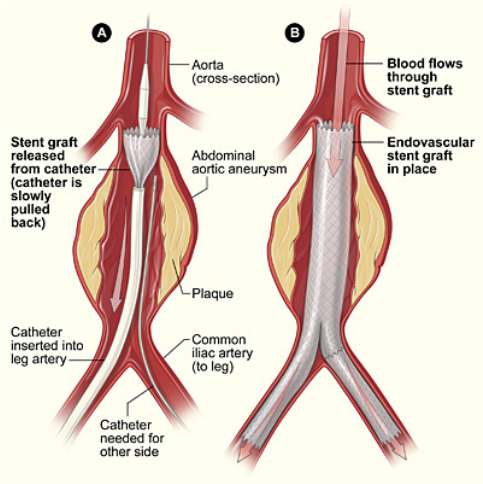


4.2 Endovascular surgery

In recent years, endovascular surgery has also become an available treatment. As with open repair, this method also excludes the aneurysm from the aortic bloodstream by attaching a graft. The procedure involves small incision in the patient's groin and the insertion of small hollow tubes called catheters into the arteries (a). The self-expanding stentgraft is moved through a sheet and passed up the pelvic arteries until it reaches the bulged area (b). The surgeon use live x-ray pictures viewed on a video screen to guide the stent graft (Norwood et al. 2007). Similar to graft in an open repair, the endovascular stent graft will also repair the blood vessels and protect against further expansion. Endovascular repair involves less blood loss, less trauma to the patient and fewer days in intensive care unit than an open repair. As the endovascular stentgrafting does not involve a large abdominal incision, the patients do also recover faster. The recovery time is usually 1-2 weeks. Endovascular repair is also associated with fewer peri-operative (within the first 30 days) complications than traditional open treatment. However, patients who are treated with endovascular stentgraft must be kept under surveillance for many years and maybe for the rest of

their lives, due to stentgraft failures which may occur years after the primary treatment (Norwood, Lloyd, Bown, Fishwick, London, & Sayers 2007).

Figure 6: Illustration of endovascular repair stent graft



Not all patients can go through with an endovascular surgery. Special morphologic[25] requirements of the infrarenal neck and iliac arteries exclude approximately 30-50% of all patients with abdominal aortic aneurysm. Hence, pre-operative CT needs to be carried out to measure lengths, diameters and angels in the different parts of the vessel (Krohg-Sørensen et al. 2002). Through open repair one can adjust and modify to accommodate varying anatomic features. On the other hand, some patients will also be inoperable for open repair, and if eligible they will be treated with endovascular surgery. These are typically elderly patients with limited life expectancy and high-risk patients with multiple co-morbidities (Green 2002;Zarins & Gewertz 2005).

[25] Morpholgy: The study of the anatomy and form of cells, organs and organism.

4.3 Treatment considerations

The recommended threshold for referring patients to repair is AAA≥55 mm. However, some patients with this size of aneurysm may be considered inoperable due to contraindications. The most common contraindications for elective repair of abdominal aortic aneurysm is myocardial infarction within the past six months, intractable congestive heart failure, intractable angina pectoris, severe pulmonary insufficiency with dyspnea at rest, severe chronic renal insufficiency and incapacitating residual effects from stroke. The risk needs to be considered for each patient, but is to a large extent disregarded in case of an emergency event (Ernst 1993).

The choice of treatment depends on many factors, such as durability, costs and mortality. Endovascular has an advantage towards open repair with respect to few peri-operative complications and shorter recovery time which will also be reflected in the costs related to shorter hospital stay. In contrast, endovascular repair will generate costs in terms of high price on implant, high preoperative costs, costs of lifelong surveillance and the need for re-interventions. The advantage of open repair is that it has been in use for more than 50 years with low failure rate. Graft failure of open repair is estimated to be as low as approximately 0.3% per year (Zankl, Schumacher, Krumsdorf, Katus, Jahn, & Tiefenbacher 2007). Available equipment and trained staff are also important considerations which need to be made prior to open surgery (Visser et al. 2007).

5. ECONOMIC EVALUATION

Elective repair is reported to be more successful than emergency repair. Hence, the preferred treatment strategy is to detect the aneurysm before it ruptures. Ultrasound screening of a population at risk has been shown to reduce the incidence of ruptured AAA, but yet there is no screening programme in Norway (Ashton, Buxton, Day, Kim, Marteau, Scott, Thompson, & Walker 2002). Ultrasound screening may be one possible strategy to reduce the overall mortality of AAA, but it needs to be evaluated.

The objective of the Norwegian health care system is to provide health services of high quality to people who are in need of health care. This aim is reflected in the health care expenditures which represents 9% of the gross domestic product in Norway (Statistics Norway 2008a). Nevertheless, there is still a gap between what is medically and technically feasible, and what is feasible with the resources available in the health care sector. Economics is based on the very fundamental assumption that resources are scarce. Hence, a decision maker who commits resources to one use will implicitly deny the use of these resources for another. There is therefore a need for economic evaluation in order to decide how to allocate resources within the health care sector.

Several policy documents have addressed the issue of priority setting in the Norwegian health care system. According to the NOU 1997:18 (“Priority setting revised”), priority settings among patients should be based on three criteria; the patient’s health condition, the expected outcome from treatment and the cost-effectiveness. The latter implies that the ratio between cost and outcome should be reasonable. The Patient Right Act of 1999 also emphasizes this view. The act expresses that a patient is entitled to necessary treatment if the expected costs are in a reasonable relationship with the effect of the intervention (1999;LOV 1999-07-02 nr 63 1999).

Economic evaluation is an aid for decision makers to address this issue. It can be defined as “the comparative analysis of alternative courses of action in terms of both

their costs and consequences" (Drummond 2005). The task is to choose among different alternative uses of scarce resources and involves identifying, measuring, valuing and comparing costs and consequences of the alternatives.

In principle, there are there are three types of complete economic evaluation; cost-benefit analysis, cost-utility analysis and cost-effectiveness analysis. The choice of approach is mainly dependent on the basis of information and how one measures the outcomes.

5.1 Cost-benefit analysis

Cost-benefit analysis is grounded in welfare economic theory. The approach requires that the consequences of the alternative programmes are valued in monetary units. All costs and consequences are expressed in comparable units, and the programmes are analysed by directly comparing the incremental costs with its incremental consequences. CBA provides information on the absolute benefit of programmes and one can assess whether a programme is worthwhile, without reference to any external standards. The main objective of CBA is to identify projects where the net social benefit is positive, indicating that a programme is worthwhile (Drummond 2005).

CBA is problematic when valuating health outcomes in monetary terms as it is difficult to assign the monetary value of health benefits. However, CBA has an advantage over CEA and CUA in that the method, in principle, has a broader scope when assigning values to the benefits. CEA and CUA are restricted to compare health programmes that assign values to health benefits such as QALYs, and their analysis mainly address production efficiency. In contrast, one may assign values to non-health related goals in CBA.

5.2 Cost-effectiveness analysis

In cost-effectiveness analysis the outcome is measured in natural units, such as avoided fractures or life years gained. The costs are related to a single, common

effect that may differ in magnitude between the alternative programmes. CEA is considered as most convenient in situations where “a decision-maker, operating with a given budget, is considering a limited rang of options within a given field” (Drummond 2005). The decision on whether a programme is worthwhile have to be made in reference to an external standard, such as budget constraints or cost-effectiveness threshold.

CEA does not use generic measure of outcome, which makes it more difficult to make a comparison across studies. However, this issue can be solved by comparing health programmes with common effect, such as life years gained (Brearly S. & Johnson J.N 2008).

5.3 Cost-utility analysis

CUA can technically be seen as a specific type of CEA. The two methods are identical on the cost side, but differ on the outcome side. CUA, in principle, measures benefits of a health care programme in terms of utility, in which the term utility refer to the preferences individuals and society may have for health outcomes (Drummond 2005). CUA presents a more convenient technique than CBA in assigning the value of health benefits, as it allows for health-related quality of life adjustments of outcomes. Simultaneously, it provides a generic outcome measure for comparison of costs and outcomes in different programmes. The health improvement is generally expressed as a common unit of measure such as quality-adjusted life-years (QALYs), disability-adjusted life-years (DALYs) or similar measures. Such effectiveness measures enable CUA to incorporate both the changes in the quantity of life, (mortality) and the changes in the quality of life (morbidity). CUA is useful when measuring the total welfare, in the sense that it enables comparison of programmes for different conditions.

CUA is in some fields considered as unethical as healthy people are given a higher weight than people with severe conditions or chronic diseases. This is also in contrast with empiric findings, reporting that people range health program that improve the

life quality of people with severe diseases above health program that improve the quality of life of relatively healthy people (Grasdal A., Askildsen, & J.E. 2003).

5.3.1 Interpretations of study findings

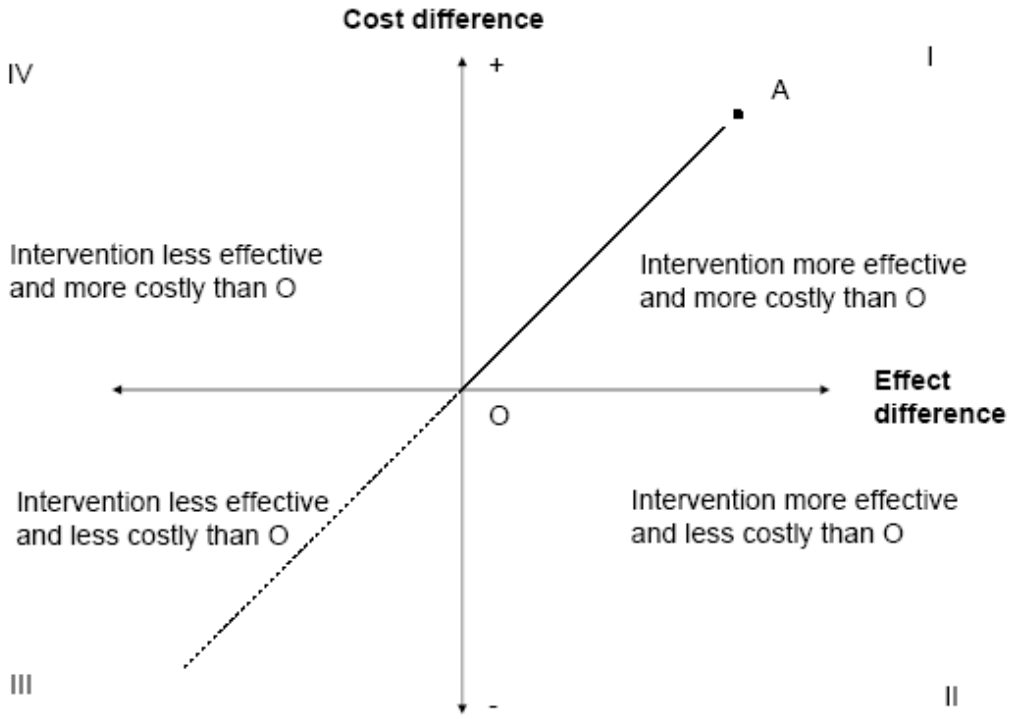
CBA is a useful technique for a decision maker to assess whether programmes are worthwhile by identifying projects where the net social benefit is positive. CEA and CUA, on the other hand, need external standards such as budget constraints or cost effectiveness ratio threshold. The decision maker uses the external standards to maximize the benefits with a given budget, by ranking the programmes according to their cost-effectiveness. The method involves examination of the additional costs (the differences in costs with or without a particular programme) that one strategy imposes over the other, compared to additional effect (the difference between a health outcome with or without a particular programme). This is illustrated in Equation 1, where C = costs and E = effects.

Equation 1:

$$ICER = \frac{C_2 - C_1}{E_2 - E_1} = \frac{\Delta C}{\Delta E}$$

When comparing the alternatives, one will consider the following four options (see Figure 8): I) Intervention is more effective and more costly than alternative O, II) Intervention is more effective and less costly than O, III) Intervention is less effective and less costly than O and IV) Intervention is less effective and more costly than O. Option II) dominates the alternatives and makes the choice more or less straightforward for the decision maker. The choice between alternative I and III will depend on the maximum cost-effectiveness ratio one is willing to accept, and is often referred to as the cost-effectiveness threshold (Drummond 2005). This value is a political or strategic value specifying the willingness-to-pay per life years gained (LYG).

Figure 7: Cost-effectiveness plane



6. RESEARCH QUESTION

Based on the previous chapters, the research question of this thesis is: Adopting a health care perspective, what are the incremental costs and health consequences of screening asymptomatic 65-year-old men for abdominal aortic aneurysm in Norway compared to no-screening?

The core issues in the economic evaluation are presented in the table below.

Table 1: Core issues in economic evaluation

Issues	
Comparators	Screenig vs. no screening
Perspective	Health care perspective
Patient group	65-year old men living in Oslo
Type of economic evaluation	Cost-effectiveness analysis performed within a Markov model
Unit costs	Hospital charges, fee schedules, wage rates in the public sectors, others
Discount rate	4%
Sensitivity analysis	One-way

7. METHODS

7.1 Model

7.1.1 The Markov model

In order to estimate the incremental costs and health consequences of a screening programme for abdominal aortic aneurysm, I chose the Markov model as a decision analytic model. A Markov model is most useful when a decision problem involves risk that is ongoing over time, the timing of events is crucial, and when events may be repetitive (Hunink 2001;Sonnenberg & Beck 1993). Abdominal aortic aneurysm is a disease which involves a continuous and increasing risk of rupture. These factors make the Markov model a more convenient way to structure the decision problem than alternatives, such as a decision tree.

7.1.2 Structure of the model

At the start of the simulation the cohort was distributed among the possible health states, and for each state the proportion of the cohort was portioned among all states according to their prevalence. The cycle length in the model was one year.

The model had two strategies; screening or no screening. Furthermore, the model assumed that a patient at any given point in time is in one, and only one, of a finite number of health states, called Markov states. Eleven health states were included:

- AAA≤30mm
- AAA 30–39 mm
- AAA 40–54 mm
- AAA 55-59 mm
- AAA≥60mm with risk factors
- AAA≥60mm with unknown risk factors

- Inoperable AAA 55-59 mm
- Inoperable AAA≥60 mm
- Post EVAR
- Dead from aneurysm
- Dead from other causes

The health states are mutually exclusive and collectively exhaustive, meaning that the patient cannot be in more than one health state at the same time, but is always in one of them.

Patients categorized in the AAA≤30 mm state were defined as healthy, while all other patients were at risk of aneurysm rupture, or had aneurysm repair. The patients in the states AAA≥30mm will either stay in the same in the same state, or grow in the aneurysm and move (transit) to another state. The transition probability is strongly dependent on the initial size of the aneurysm and once an aneurysm greater than 55 mm is detected, the patient will be referred for either elective endovascular or elective open repair. Detected aneurysms under this threshold are subject to a monitoring programme.

Some patients will however, for various reasons, be unsuitable for surgery and were categorized as inoperable. These patients are denied surgery because they have certain risk factors (see chapter 4) which will make it too risky for them to undergo a surgery. Patients in this state will be monitored until the aneurysm attains a diameter at which the risk of rupture is thought to outweigh the operative risk. Although being monitored, some of these patients will experience a rupture of the aneurysm, and will have to undergo an emergency surgery.

Patients who were not included in a screening programme were assumed to be similar to those in the screening group, regarding risk of the different events. Some of the patients in the non-invited group will also have their aneurysms detected incidentally through physical examination or routine medical test. These patients will be included

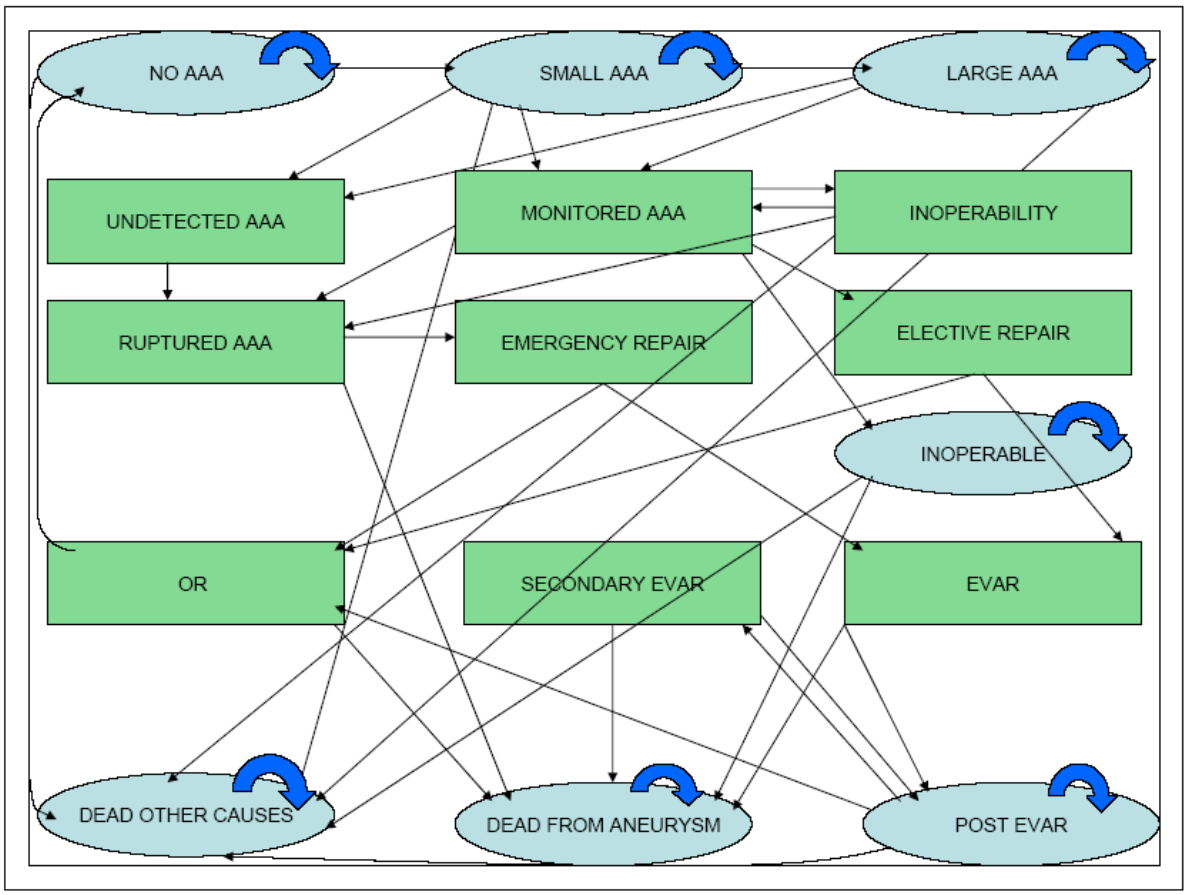
in the same monitoring programme, as those who were attending the screening programme in the first place.

Patients undergoing a repair will either survive or die. Patients who undergo an open repair will transit to AAA≤30mm and were defined as healthy. Patients experiencing a successful endovascular repair will also be defined as healthy, but due to the acquired post-operative monitoring programme described in chapter 4, they will transit to the Post EVAR state. These patients differ from patients who have undergone a successful open repair, because they more frequently experience post operative complication and must be kept under surveillance. Some patients in the Post EVAR state will also transit to the Secondary EVAR state. These patients may have complications that require a second intervention. The re-intervention may for some patients involve only a small adjustment of the graft, while others are be referred for a new surgery and this time they will be referred to open repair. By defining these patients in a separate state, one solves the Markov property problem by assuming that the process has no memory for earlier cycles. If the repair was successful they will transit to AAA≤30mm.

The model consisted of two death states in which the whole cohort ends after a sufficient number of cycles. Patients who die from AAA before surgery or do not survive a repair will end up in the state “Dead from aneurysm”, while “Dead other causes” refers to non-AAA causes of death. The death stat are so-called absorbing state because once a patient reaches this state, he or she cannot leave this state, but will remain there.

The state-transition diagram below illustrates the possible health states, events and transitions. The oval named “no AAA” refers to the AAA≤30 mm state, while the oval named “small AAA” refers to the health state AAA30-39mm and 40-54 mm. The “large AAA” includes AAA 55-59 mm and AAA≥60 mm.

Figur 8: Model structure



The ovals represent the health states, while the rectangles represent the events. The arrows show the possible transitions for the patient.

7.1.3 Validation of the model

In order to validate the model, I used data from Statistics Norway to compare the remaining life expectancy in the population to the remaining life expectancy predicted by the model.

An important assumption made in discrete-time Markov models is that all state transitions occur simultaneously, at the end of each cycle. In reality, however, most kinds of transitions occur gradually throughout a time interval and on average half-way through (TreAge Software 2007). This assumption may result in overestimation of expected survival in the model. Hence, in order to compare the remaining life

expectancy in the population, based on data from Statistics Norway, to the remaining life expectancy predicted by the model, I implemented the half-cycle correction in the TreeAge Software. This adjustment allows you to divide every alive state's incremental reward in half, and assign the half reward as its initial and final reward

In addition, I compared the number of AAA-related deaths as predicted by the model with those reported to Statistics Norway.

7.2 Litterature search

A systematic review of the literature was conducted to get an overview of relevant aspects of the disease and the decision problem. The searches were undertaken January through May 2008 using the PubMed database. In general I used the key words *abdominal aortic aneurysm, screening and cost-effectiveness.* These key words were separately combined with additional terms such as *epidemiology, prevalence, incidence, sensitivity, specificity, treatment, risk factors, risk of rupture, expansion rate, natural history, costs, and ethics.* Additionally, relevant references mentioned in the identified studies were explored. No publications were scrutinized by more than one student. Each Pubmed hit was studied with respect to relevance of title, and the abstract read in full if the title was relevant. When the title was relevant, full text articles were obtained.

7.3 Probabilities

The probabilities used in this analysis are mainly collected through my literature search. Since my literature search revealed few Norwegian articles on abdominal aortic aneurysm, most of the probabilities used in this analysis are collected from articles published outside Norway. However, I have when possible, used data collected in Norway. When not, data were collected from countries in which the patients with the disorder and its natural course are in a comparable position. Furthermore, all probabilities are evaluated by a medical expert opinion and

supplemented when needed. All probability parameters included in the model are reported in Appendix I.

7.3.1 Prevalence of detected abdominal aortic aneurysm

The Tromsø Study was the only Norwegian population-based study that has investigated the prevalence of AAA, that my literature revealed (Singh, Bonaa, Jacobsen, Bjork, & Solberg 2001). However, the study does not report detailed information on the size of the aneurysm. Hence, I collected these numbers from the MASS-study , supplemented with findings from Lederle and co-workers , Scott and co-workers and Henrikson and co-workers (Ashton, Buxton, Day, Kim, Marteau, Scott, Thompson, & Walker 2002;Henrikson M. & Lundgren F. 2005;Lederle et al. 1997;Scott, Ashton, & Kay 1991). The prevalence, in terms of size of aneurysm, is presented in Table 2.

Table 2: Prevalence of AAA according to size from screening studies

Variable	Base Case Value	Range	Reference
AAA ≤ 30 mm	0.9671	0.91-0.99	Henrikson et.al. (2005)
AAA 30-39 mm	0.02	0.02-0.03	Scott et.al.(1991), Ashton et.al. (2002)
AAA 40-54 mm	0.008	0.006-0.014	Scott et.al.(1991), Ashton et.al. (2002) Lederle et.al. (1997)
AAA 55-59 mm	0.003	0.002 0.0049	Scott et.al.(1991), Ashton et.al. (2002), Lederle et.al. (1997)
AAA ≥ 60 mm	0.0019	0.0019-0.003	Scott et.al.(1991), Lederle et.al. (1997)

These values are derived through population-based studies where people have been screened. Hence, in order to consider these as prevalence numbers one needs to assume that the screening devices produce sensitivity and specificity values close to 100 %, meaning that everyone that has an aneurysm larger than 30 mm will be detected.

The non-screened patients who are not subject to screening will have their aneurysms detected incidentally through physical examination or routine medical test. The

literature indicates that the yearly probability of being detected opportunistically range from 0.051(Henrikson et.al:2005) and 0.125 (Kim et al. 2007). The range is relatively wide, and may be explained by the correlation between the size of the aneurysm and the detection rate. Hence, in the analysis I assumed that detection rate increases with the size of the aneurysm. This can also be supported in the literature on diagnosis of AAA referred to in chapter 3.

7.3.2 Rupture

Several studies report the yearly probability of rupture. As the probability increases with age, the studies also provide size dependent rupture rates. Within each size range, the probabilities vary slightly. One explanation for this variation may be different age structures in the studies. The probability of rupture is also gender dependent and may therefore result in variation in the probabilities. Size dependent rupture rates are presented in Table 3.

Table 3: Rupture rate according to size from screening studies

Variable	Base Case Value	Range	Reference
AAA 30-39 mm	0.003	0.002-0.009	Brown et.al:2003, Vardulaki et.al:1998
AAA 40-54 mm	0.01	0.006-0.027	Vega et.al:2006, Brown et.al:2003, Henriksen et.al:2008
AAA 55-59 mm	0.065	0.05-0.11	Green et.al:2006, Zankl et.al:2007, Bergquist et.al:2002
AAA ≥ 60 mm	0.156	0.10-0.191	Brown et.al:2003, Bergquist et al:2007, Lederle et al:2002, Brown

7.3.3 Background mortality

Age and gender specific mortality for all causes from 2002 were used as background mortality. Due to lack on data on non-AAA mortality for patients who are inoperable from AAA, I used data for mortality among patients with cardiovascular diseases. These rates are reported from Statistics Norway and can be found in Appendix 4.

7.3.4 Clinically effectiveness

Until recently, the research on clinical effectiveness has mostly been concentrated on specific aspects on the treatment strategies. Furthermore, when endovascular repair became an available method most research has been dedicated on this method. Information on the effectiveness has relied upon voluntary registers such as the UK Registry for Endovascular Treatment of Aneurysms and the European Collaborators on Stent Graft Techniques for Abdominal Aortic Aneurysm Repair Register.

However, in recent years several controlled trials of endovascular repair against open repair have been initiated. In UK there are two multi centre trials (EVAR1 and EVAR2), which started in 1999 and in The Netherlands there is also a smaller trial called DREAM. The EVAR 1 Trials investigated patient at the age of at least 60 years old with a diameter of 55 mm or more. They found a 30-day mortality of 1.5% and 5.8% for endovascular repair and open repair respectively. The DREAM trial found similar numbers, reporting a 30-day mortality of 1.2 % for endovascular repair and 4.6 % for open repair (Greenhalgh et al. 2004;Prinssen, Buskens, & Blankensteijn 2002). The mortality rates vary to some extent between the studies, but most studies report that the mortality rate for open repair is slightly higher than for endovascular repair.

The mortality risk related to emergency repair, are mainly estimates from observational studies. From my literature search I found mortality risks varying from 30% (Ashton, Buxton, Day, Kim, Marteau, Scott, Thompson, & Walker 2002;Silverstein, Pitts, Chaikof, & Ballard 2005) to 75% (Silverstein, Pitts, Chaikof, & Ballard 2005). This wide range may be explained by the complexity of a rupture situation. Depending on the circumstances for the patient who experiences the rupture, one will experience different mortality risks. However, most clinical guidelines operate with a mortality risk of 50% for both endovascular repair and open repair. This is also the value I used in my model.

7.4 Costs

The cost estimating process in economic evaluation consists of three phases: identification of the types of resources used in the health programme, quantification of the cost components, and valuation of the components (assigning a monetary value for each component).

In the identification phase the costs relevant to the chosen perspective is identified. In my analysis I excluded all indirect costs related to productivity loss and time consumption of the patient and family members (Time consumption of the patient is included in the sensitivity analysis) (Drummond 2005). Hence, this analysis identifies the resources from a health care perspective because of limitations of available data.

The identification and quantification of costs included in the model were based on discussions with vascular surgeons at Aker University Hospital. With respect to valuation and unit costs, I have used data from the Norwegian Medical Association, The Norwegian Ambulance Association, Capio Diagnostic and The Norwegian Labour and Welfare Administration.

In order to reflect a positive rate of time preference, the costs were discounted. The Norwegian Ministry of Finance suggest using discount rate between 2.5-5% for economic evaluation (The Norwegian Ministry of Finance 2005). I discounted at 4% in my analysis. All costs were measured in Norwegian Kroner (NOK) and the ranges of upper and lower bounds were determined by the base case value +/- 20 % rate. The costs are presented in Table 5.

7.4.1 Cost of screening programme

The screening programme will generate costs from particularly two components. That is the cost of screening patients and the cost of monitoring them.

Cost of screening

The cost of screening includes the cost of inviting the target individuals, including the administration costs and the cost of the invitation, and the ultrasound examination

cost. No screening programmes for AAA exist in Norway today, and I assumed that the administrative costs will be equal those of an ongoing programme for colorectal cancer (NOK160 per patient, Eline Aas, University of Oslo, personal communication). Furthermore, I used experiences from screening programmes for AAA in Sweden (Ashton, Buxton, Day, Kim, Marteau, Scott, Thompson, & Walker 2002;Henrikson M. & Lundgren F. 2005). The unit cost of the ultrasound examination was based on the NAV[26] fee schedule (NOK347 + NOK200 in patient co-payment) which represent in principle 40% of the total costs to society.

Cost of monitoring

The monitoring cost depends on the size of the detected aneurysm. Based on expert judgment, I assumed that patients with an AAA 30-54 mm will be examined once a year. Patients with AAA 55-59 mm will be examined twice a year, while patients who have AAA≥60 mm will be examined four times a year. This is partly due to the risk of rupture, but also motivated by the other risk factors. The examination consists of an ultrasound examination and a visit at the out-patient-clinic. NAV report that the unit cost of an out-patient-clinic visit is NOK700.

7.4.2 Cost of rupture

In case of rupture, the patients will need a home visit from their general practitioner, in addition to ambulance transport to the hospital. Some will also reach emergency repair. The ambulance cost was derived from The Norwegian Ambulance Association and the latest available unit cost is reported to be NOK9500. In order to calculate the cost of GP home visit, I used fee schedules from the Norwegian Medical Association. Under the assumption that an ordinary patient visits their GP four times per year, I divided the fixed per-patient fee by four and added the price of fee-for-service of the home visit.

[26] The Norwegian Labour and Welfare Administration.

Not all patients reach surgery, but if they reach the hospital they will be examined with ultrasonography and in some cases also computed tomography. Vascular surgeons at Aker Hospital assume the fraction of patients who will need CT to be 90%.

7.4.3 Cost of repair

I included two methods of repair; open repair and endovascular repair. The costs are higher for endovascular repair than open repair in terms of higher per-operative and examination costs after discharge from hospital (see Appendix II). However, within each method the peri-operative costs will be equal whether it is an emergency or elective repair. The cost difference between emergency and elective repair, however, is identified through the pre-operative and post-operative costs. In distinction to the pre-operative costs of an emergency repair, which preliminary consist of US examination, the costs of an elective repair will also consist of a CT examination and an out-patient-clinic visit. The unit cost of a CT examination and an out-patient-clinic visit is reported in the NAV database to be NOK687 and NOK700, respectively.

The post-operative costs between emergency and elective repair differ, as the number of days in the intensive care and ward unit is less for elective repair than emergency repair. This is illustrated in table 4. Furthermore, patients who are referred for an elective repair do also have a higher probability of successful repair than those referred for emergency. These patients will not only generate post-operative costs in terms of hospital stay, but will also need examinations after discharge from hospital shown in Appendix II. The cost of secondary interventions is also reported in Appendix II.

Table 4: Post-operative costs

Post-operative costs (NOK)			
Cost item	**Elective repair**	**Emergency repair**	**Source**
Intensiv care unit			
Number of days after endovascular repair	0.5	1	AUH
Number of days after open repair	2	4	AUH
Cost per day	18525	18525	AUH
Total cost intensive care unit	**46313**	**833623**	
Ward unit			
Number of days after endovascular repair	3	4	AUH
Number of days after open repair	5	6	AUH
Cost per day	8025	8025	AUH
Total cost ward unit	**64200**	**72225**	
Total post-operativ costs	**110512.5**	**155588**	

Table 5: Cost components included in the mode[27]

Cost components included in the model			
Model parameter	**Description**	**Base case value**	**Sources**
cAneurysmElEVAR	Cost of death from elective EVAR	111755[7]	AUH, CD, NAV
cAneurysmElOR	Cost of death from elective OR	20857[8]	AUH, CD, NAV
cAneurysmEmEVAR	Cost of death from emergency EVAR	109521[9]	AUH, CD, NAV
cAneurysmEmOR	Cost of death from emergency OR	18623[10]	AUH, CD, NAV
cAneurysmSecEVAR	Cost of death from secondary EVAR	26967[11]	AUH, CD, NAV
cAneurysmSecOR	Cost of death from secondary OR	19810[12]	AUH, CD, NAV
cInHospital	Cost of ruptured AAA which does not reach surgery	965[13]	AUH, CD, NAV
cMon2	Cost of monitoring AAA 30-39 mm	1547[14]	AUH, CD, NAV
cMon3	Cost of monitoring AAA 40-54 mm	1547[15]	AUH, CD, NAV
cMon4	Cost of monitoring AAA 55-59 mm	3094[16]	AUH, CD, NAV
cMon5	Cost of monitoring AAA > 60 mm	6188[17]	AUH, CD, NAV
cPostEVAR	Cost of Post EVAR-programme	950[18]	AUH, CD, NAV
cRupture	Cost of rupture	9953[19]	AUH, CD, NAV, NMA, NAA
cScreening_programme	Cost of screening programe	1007[20]	AUH, CD, NAV, EA, Henriksen (2005)
cSuccessElEVAR	Cost of successful elective EVAR	228590[21]	AUH, CD, NAV
cSuccessElOR	Cost of successful elective OR	132770[22]	AUH, CD, NAV
cSuccessEmEVAR	Cost of successful emergency EVAR	271431[23]	AUH, CD, NAV
cSuccessEmOR	Cost of successful emergency OR	175611[24]	AUH, CD, NAV
cSuccessSecEVAR	Cost of successful secondary EVAR	143802[25]	AUH, CD, NAV
cSuccessSecOR	Cost of successful secondary OR	130536[26]	AUH, CD, NAV

[7] NOK2234 (cPreEVAR) + 109521 (cPeriEVAR) =NOK111755
[8] NOK2234 (cPreOR) + NOK18623 (cPeriOR) = NOK20857
[9] NOK109521 (cPeriEVAR)
[10] NOK18623 (cPeriOR)
[11] NOK1187 (cSecPreEVAR) + NOK25780 (cSecPeriEVAR) = 26967
[12] NOK1187 (cSecPreOR) + NOK18623 (cPeriOR) = 19810
[13] NOK 347 (cUltrasound) + 0.9 x NOK687 (fCT x cCT) = NOK 965
[14] NOK 347 (cUltrasound) + NOK 500 (cCo-payment US) + NOK 700 (cOut-patient-Clinic) = NOK1547
[15] NOK 347 (cUltrasound) + NOK 500 (cCo-payment US) + NOK 700 (cOut-patient-Clinic) = NOK1547
[16] 2 x [NOK 347 (cUltrasound) + NOK 500 (cCo-payment US) + NOK 700 (cOut-patient-Clinic)] = NOK3094
[17] 4 x [NOK 347 (cUltrasound) + NOK 500 (cCo-payment US) + NOK 700 (cOut-patient-Clinic)] = NOK6188
[18] NOK 347 (cUltrasound) + NOK103 (cX-ray overview) + NOK500 (cCo-payment) = NOK950
[19] NOK370 (cGP homevisit fee) NOK 87 (1/4 of capitation fee)+ NOK9500 (cAmbulance) = NOK9953
[20] NOK347 (cScreening Ultrasound examination) + NOK500 (cCo-payment) + NOK160 (cInvitation_Administration = NOK1007
[21] NOK2234 (cPreEVAR) + NOK109521(cPeriEVAR) + NOK110512,5 (cPostElEVAR) + NOK6322,5 cPostExamEVAR = NOK228590
[22] NOK2234 (cPreOR)+ NOK18623 (cPeriOR) +110512,5 (cPostElOR) + 1400 (cPostExamOR) = NOK132770
[23] NOK109521(cPeriEVAR) + 155587,5 (cPostEmEVAR) + 6322,5 (cPostExamEVAR) =NOK271431
[24]NOK18623 (cPeriOR) + 155588 (cPostEmOR) + 1400 (cPostExamOR) = NOK175611
[25] NOK1187 (cSecPreEVAR) + NOK25780 (cSecPeriEVAR) + NOK110512,5 (cPostElEVAR) + 6322,5 (cPostExamEVAR) = NOK143802
[26] NOK18623 (cPeriOR) + 110512,5 (cPostElOR) + 1400 (cPostExamOR) = NOK130536

[27] Description of source abbrivation: AUH = Aker University Hospital, CD = Capio Diagnostic, NAV = The Norwegian Labour and Welfare Administration, NMA = Norwegian Medical Association, NAA = Norwegian Ambulance Association, EA = Expert opinion from Eline Aas

7.5 Cost-effectiveness threshold

The decision on whether or not do adopt a screening programme should in principle be determined by the cost-effectiveness threshold. The Norwegian Ministry of Finance declares that the cost-effectiveness threshold represents the maximum value that the society is willing to spend in order to gain one unit of health benefit (The Norwegian Ministry of Finance 2005). The threshold value in this analysis is based on the suggestion from the Norwegian Directorate of Health. They suggests the threshold to be NOK500 000 per LYG. Previously, the Ministry of Finance has suggested a threshold of NOK425 000 while Kristiansen and Gyrd-Hansen proposed NOK350 000 (Kristiansen & Gyrd-Hansen 2007;The Norwegian Ministry of Finance 2005).

The benefit of such threshold is that it may help decision makers to give lower priority to interventions with small health benefits and high opportunity cost. Although the cost-effectiveness threshold is a tool to help us determine whether or not to offer an intervention, other factors than economic efficiency also needs to be considered. When setting priorities, decision makers need to evaluate other issues such as ethics and equity. Hence, when one include these aspects in the evaluation, there will sometimes be good reasons for offering an intervention that has greater costs than NOK500 000 per life year gained, and there will also be good reasons not to offer an intervention that is cost-effective.

8. RESULTS

8.1 Cost and health consequences

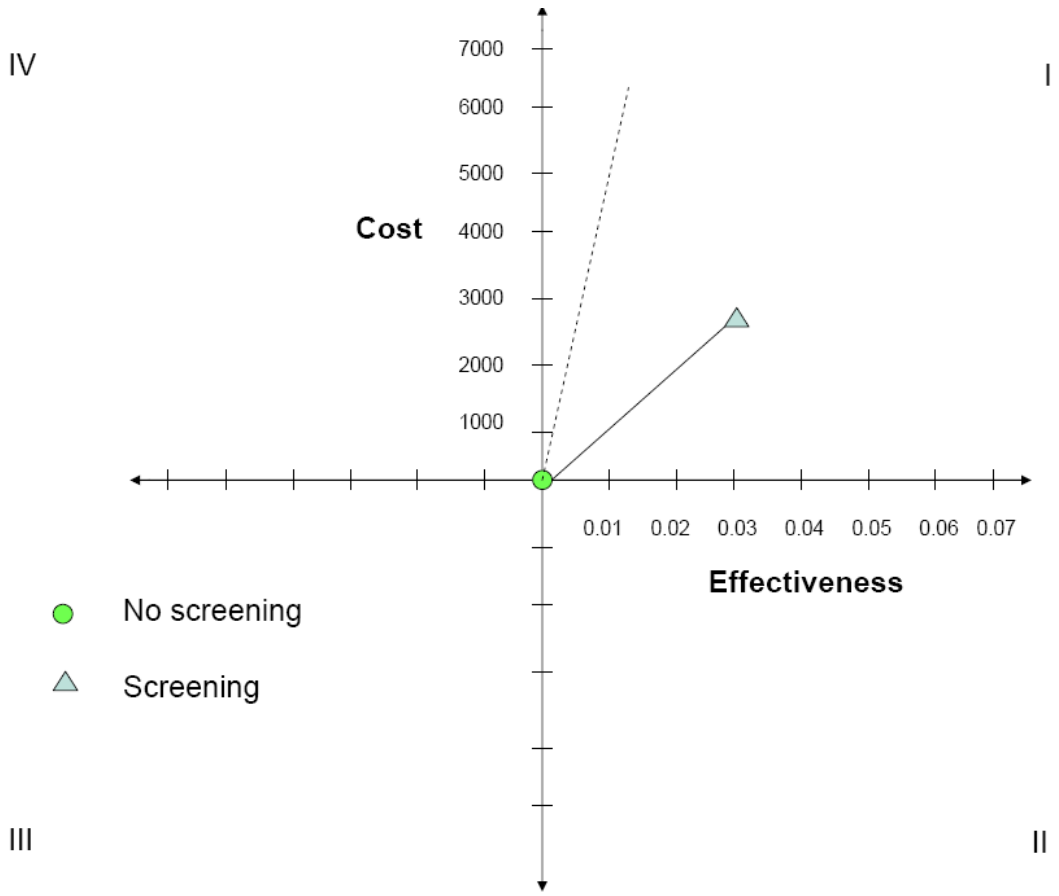
The average life time AAA-related cost of a 65-year-old patient in the non-screening group was NOK3010 (NOK2032 discounted) and NOK6074 (NOK4686) discounted in the screening group, resulting in incremental costs of screened patients of NOK2677 per patient. The life expectancy of a non-screened patient is 16.3832 years (11.7051 years discounted), while it was 16.4351 (11.7345 discounted) for a screened patient. The incremental life year gained was 0.029 which implies NOK90200 per additional life year gained. The model indicates that the life time risk of dying from AAA is 0.003 when screening is undertaken, compared to 0.008 when it is not (63 % reduction in AAA-related deaths). The main findings are presented in the Table 6.

Table 6: Cost and consequences for AAA. All cost (Norwegian Kroner (NOK) 2007) and life years discounted at 4%.

Strategy	Cost	Incr. cost	Effect	Incr. eff	C/E	ICER
No screening	2032		11.7051		174	
Screening	4686	2654	11.7345	0.0294	399	90300

The results are shown in Figure 10, by means of the cost-effectiveness plane of the programme options. The slope of the line indicates the ICER.

Figure 9: Cost-effectiveness plane of the programme options



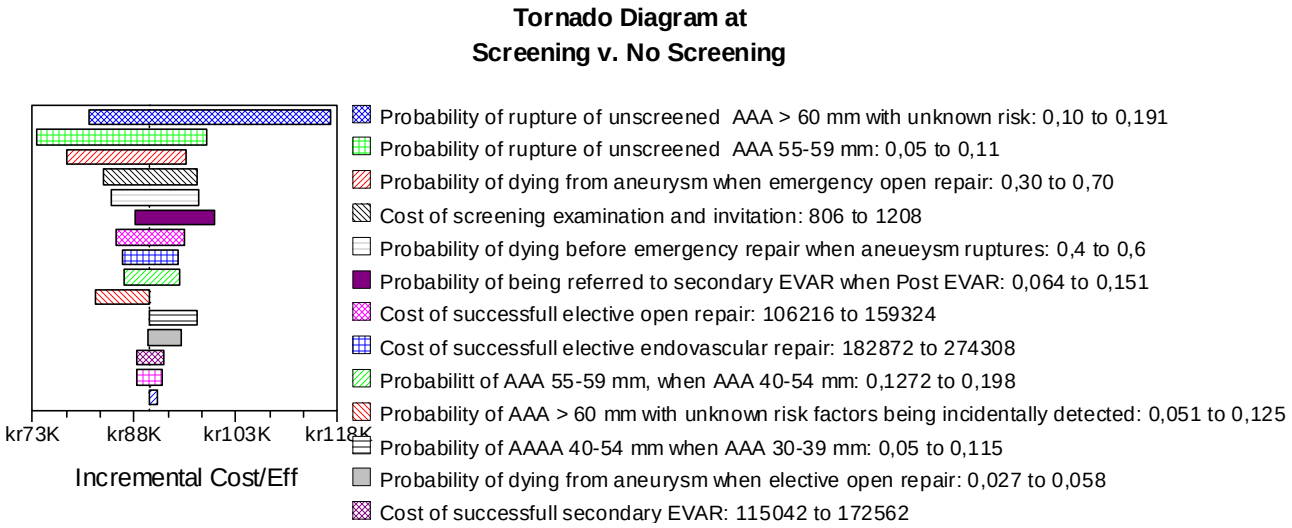
8.2 Sensitivity analysis

Due to uncertainty in the parameter values, one-way sensitivity analyses were performed for all parameters, to examine whether the conclusion would be altered by any realistic change in the parameter values (see Appendix III). The sensitivity analyses showed that the probability of rupture of unscreened AAA≥60 mm with unknown risk factors, the probability of rupture of unscreened AAA 50-59 mm, the probability of dying from aneurysm when emergency open repair and the cost of screening and invitation were the variables that had the greatest impact on the results,

but none of this uncertainty is large enough to threaten the conclusion that screening for AAA is cost-effective (see Figure 11). For example, if the probability of rupture of unscreened AAA≥60 with unknown risk factors was 0.1 (lower bound) it would result in an ICER of NOK81064 and if the probability of rupture of AAA 40-54 mm was 0.191 (upper bound) it would result in an ICER of NOK116844. If the cost of screening and invitation was reduced to NOK806 (lower bound) it would result in an ICER of NOK83435 and if the cost of screening and invitation was increased to NOK1208 (upper bound) it would result in an ICER of NOK97109.

In general, the sensitivity analysis showed that the conclusion is less threatened by uncertainty in parameters partly based on assumptions, and more sensitive by parameters that were collected from published results.

Figure 10: Tornado diagram of the most sensitive parameters



8.3 Validation of the model

Statistics Norway reports that the remaining life expectancy for 65-year-old men was 15.929 in 2005 (see Appendix V), while the remaining life expectancy predicted by the model is 15.885 resulting in a difference of 0.044 (Statistics Norway 2002a).

Statistics Norway reports that the number of AAA-related deaths was 106 in 2005(Statistics Norway 2005b). The model predicts that the life time risk of dying from AAA is 0.008. In 2008 the number of number of 65-year-old men in Norway was 21057 (Statistics Norway 2008b). Assuming constant population cohort and mortality, the model predicts that the number of AAA-related deaths is 168.

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9. DISCUSSION

The results of this model indicate that screening for AAA may be a cost-effective technology. This conclusion, however, should be seen against the methodological limitations of the study, and the findings of other studies.

9.1 Metholodical limitations

9.1.1 Source of probabilities

Since my literature review revealed few articles published in Norway, I had to collect most of my data from articles published in other countries. The collected articles were published in Western countries and, hence, there is no reason to believe that Norway differs considerable with regards to demography, epidemiology and clinical practice compared to these countries. However, demographic differences, such as distance to the nearest hospital, may cause some differences in the results. The population in Norway experience a longer distance to the nearest hospital compared to people in most other industrialised countries, in which the population density is higher. The probability of dying from rupture is therefore likely to be higher in Norway. This difference will tend to make the benefit of screening in Norway greater than the model would predict.

Natural course of AAA is difficult to study and information on some probabilities is scarce. Some of the included probabilities were therefore based on assumptions and variation, and uncertainty in these parameters may affect the main result. However, the sensitivity analyses implicate that the conclusion is less sensitive to variation in these parameters than those collected from published results.

9.1.2 Source of costs

The identification and quantification of the costs included in the model were made through discussions with vascular surgeons at Aker University Hospital. In order to valuate the cost components I also used data from Norwegian Medical Association,

The Norwegian Ambulance Association, Capio Diagnostic and The Norwegian Labour and Welfare Administration. The valuation of the cost of a day of institutional care can be specific troublesome, in that the use of an average cost per day is calculated on the basis of the institution's entire annual case-load (Drummond 2005). This may cause bias of the actual cost estimates for the specific condition. In order to identify all important costs, measure them accurately in appropriate physical units, and value them credibly, one should seek to cost collect data from empirical studies of representative patient group. Due to time limitations, this was not feasible for my model.

9.1.3 Background mortality

Age and gender specific mortality for all causes and cardiovascular diseases were collected from 2002 (Ashton, Buxton, Day, Kim, Marteau, Scott, Thompson, & Walker 2002;Scott, Wilson, Ashton, & Kay 1995;Statistics Norway 2002b). However, there is little reason to believe that the mortality rates of men 65-100 years have changed significantly since 2002.

Information obtained from studies of patients unfit for repair is incomplete. In order to find data on non-AAA mortality for patients who are inoperable from AAA, I therefore used national data for mortality among patients with cardiovascular diseases. This assumption may results in a shortened remaining life expectancy as the total mortality risk for cardiovascular diseases is higher than for patients considered unfit for repair of AAA. However, this assumption may be reasonable as these patients also have a risk of dying from other causes than cardiovascular diseases, such as cancer and kidney diseases.

9.1.4 Attendance rate

The model assumed 100% attendance rate from the invited men. Excluding attendance rate may cause bias in the model, because a lower attendance rate means that the average screening cost per patient will be higher. However, several studies

have shown that the attendance rate have little effect on the cost-effectiveness ratio (Boll et al. 2003;Wanhainen et al. 2005).

An important issue when discussing the attendance rate of a screening programme is the selection bias of the people who choose to attend. Several studies indicate that the people who attend screening are healthier than those who not attend(Ashton, Buxton, Day, Kim, Marteau, Scott, Thompson, & Walker 2002;Scott, Wilson, Ashton, & Kay 1995). The life expectancy of screened patients is considered as a key variable for the cost-effectiveness ratio, and hence the cost-effectiveness may be high, despite a low attendance rate.

9.1.5 Cost of repair

In addition to exclude all indirect costs related to productivity loss and time consumption of the patient and family members, I also excluded indirect costs related to the treatment. Another important exclusion was training costs. The training of students and house physicians takes place in the day time. Hence, in case of an emergency repair the cost of repair will be higher if the repair takes place in the day time compared to in the night. This exclusion was made due to lack of data, as the time limitation did not allow me to do a counting on how many repairs that take place in the day time and in the night.

Another limitation of the model is the exclusion of helicopter cost, in case of a rupture. My model considers a cohort of 65-year-old men in the district of Oslo. The people in Oslo live closer to the nearest hospital than people in the rest of the country. Hence, in case of a rupture the men will be transported with ambulance and not helicopter as one will need in places with wider distances.

The exclusion of training cost and helicopter cost, reduce the cost of emergency repair which makes the cost-effectiveness of screening less optimistic.

9.1.6 Rupture rate

My literature search did not reveal articles on age-specific rupture rates. I therefore had to collect probabilities from various articles. Each of them only investigates a limited age group of the defined cohort in my model (men between 65 to100 years) and not the total group. There is reason to believe that demographic and epidemiological differences between the cohorts may cause uncertainties in the included probabilities on rupture. However, none of the revealed articles from my literature search investigated the rupture rate of the men in the very upper bound of the cohort. As the risk of rupture increases with age, there is therefore no reason to believe that my model overestimates the risk of rupture.

9.1.7 Exclusion of women

The model did not include women. One may argue that excluding women is discriminating as women are also at risk of AAA. However, epidemiological studies report that the incidence and prevalence among women is significantly lower than among men (Lederle, Johnson, Wilson, Chute, Littooy, Bandyk, Krupski, Barone, Acher, & Ballard 1997;Singh, Bonaa, Jacobsen, Bjork, & Solberg 2001). Previous cost-effectiveness studies have concluded that the incidence have an effect on whether screening is considered as cost-effective, but screening women have also shown to be cost-effective (Cosford & Leng 2007;Wanhainen et al. 2006).

9.2 Strengths of the study

My literature search did not reveal any cost-effectiveness studies which were based on Norwegian cost data. Furthermore, none of them included both endovascular and open repair as treatment options. As I have included Norwegian cost and considered both methods in my analysis, this study may add new information to the research field.

9.3 Findings of other cost-effectiveness studies

In order to validate the structure of the model, it is important to make a comparison with results from other studies. When comparing studies, it is important to keep in mind that the choice of input may have a large impact on the results. Particularly comparison between countries may differ with regard to demography, epidemiology and clinical practice (O'Brien 1997).

No cost-effectiveness analyses for Norway have been identified. Hence, I had to compare my results with studies from other countries. In my study I captured both open repair and endovascular repair as treatment options. The studies identified in Medline did only include one method. The two treatment methods involve a significant difference in cost, and may create different ICERs.

Previous randomized controlled trials and non-randomized controlled trials indicate that screening men for AAA is cost-effective. Over a 4-year period Lindholdt and co-workers (Lindholt et al. 2006) screened men aged 64-73 in the Viborg County in Denmark. 12,639 men were randomly selected to be invited for screening or not. Through ultrasound examination the study team detected men with aneurysm defined as AAA larger than 30 mm. During four years from the randomization there were 9 AAA-related deaths in the screening group compared to 27 in the control group, resulting in a 67 % reduction of AAA mortality during the first 52 months after randomization. The estimated cost per saved life year was DKK 20 656. The study indicates a substantial long term benefit of screening for AAA.

Wilmink and co-workers (Wilmink et al. 2003) invited men in the Huntingdon District in UK for screening between 1991 and 1998. 50-year-old men were invited for screening for abdominal aortic aneurysm. During the study period, 71 deaths occurred as a result of ruptured AAA. 17 of the deaths were in the screening group, while 54 were in the control group. The screening programme resulted in 51 life-years gained per year and a cost per life-year of $ 1173. Wilmink and co-workers conclude that screening for AAA can be cost-effective in populations in which

incidence of ruptured aneurysm, in the absence of screening, is more than 5 per 10000 person-years, and if screening can reduce the incidence by at least 50%.

Other randomized clinical trials report that the program reduces the AAA-related mortality, but the reduction was not statistically significant. Scott and co-workers (Scott, Wilson, Ashton, & Kay 1995) report that a screening programme reduces the mortality by approximately 50 %, while Norman and co-workers report that the age standardized mortality for those who actually attended the screening was 60 % lower in the control group (Norman, Jamrozik, Lawrence-Brown, Le, Spencer, Tuohy, Parsons, & Dickinson 2004).

Boll and co-workers (Boll, Severens, Verbeek, & van, V 2003;Norman, Jamrozik, Lawrence-Brown, Le, Spencer, Tuohy, Parsons, & Dickinson 2004) designed a Markov model to compare the effects of a single screening for a cohort of men 60-65 years in the Netherlands with the current no screening strategy. The life expectancy for men 60-65 years without screening was estimated to be 16.99 years beyond their current age. The model calculated that the life expectancy for the men who were screened was 17.27 years, resulting in an average prolongation of life of 0.28 year. This life extension due to mass screening of AAA caused a cost of €334 resulting in a cost of €1193 per life year gained. Boll and co-workers conclude that screening for AAA appears to be worthwhile.

While all studies conclude that screening for AAA is cost-effective for men, the ICERs vary somewhat because of differences in study design and parameter values.

9.4 Validation of the model

The remaining life expectancy predicted in the model is somewhat lower that the reported remaining life expectancy reported from Statistics Norway. When evaluating the validation of the model, I want the predicted remaining life expectancy from the model to be close to equal to the reported remaining life expectancy reported in Statistics Norway. I found that the difference between the prediction of the model and Statistics Norway is 0.044. This difference can partly be explained by the assumption

made on the non-AAA mortality of inoperable patients. With available data we would probably have experienced a smaller difference, but one can argue that the model still predicts valid information on the population.

Regarding the AAA related deaths, the model predicts 168, while Statistics Norway report 106. In chapter 2 I discussed the estimates of AAA mortality and argued that the reported mortality may be hampered by low rates of post mortems. From this argument, one would expect that the model would predict a higher number of AAA related deaths than 168. The predicted mortality from the model may be explained by too low included probabilities of AAA and AAA mortality. This may tend to make the benefit of screening in Norway greater than the model would predict.

9.5 Policy implications and conclusion

My results indicate that screening 65-year old men for abdominal aortic aneurysm is cost-effective. The sensitivity analyses also indicate that the result is not threatened by any realistic change in all variables. Based on the criteria presented in chapter 5, I conclude that screening 65-year-old men for this disorder fulfil the cost-effectiveness criteria in the priority setting guidelines discussed in chapter 7.5. However, cost-effectiveness is not the only criterion that should be fulfilled. As presented in chapter 3, WHO has defined screening as a medical investigation that does not arise from a person's request for advice for specific symptoms or complaints. Hence, they recommend that the following basic criteria should be fulfilled:

1. <u>The disease should be an important health problem:</u>

In chapter 2 I presented the epidemiology of AAA, showing that the disorder is the cause of 1.3% of all deaths among men in the age of 65-85 in developed countries. Among elderly men it may cause as many as 2% of all deaths, and it is also likely to assume that magnitude of the health problem is underestimated (Earnshaw et al. 2004). Due to low prevalence of AAA, women are generally not considered as suitable target group for AAA screening.

2. A generally acceptable method of treatment must be available:

In chapter 4 I presented the available treatment methods for AAA. I will not go further into the methods, but both open repair and endovascular repair are effective and extensively used. Open repair is considered as the gold standard, as there is still more to be learned about the endovascular technique with regards to complications, follow-up routines and re-interventions (Bergqvist, Bjorck, & Wanhainen 2008). However, according to the Norwegian Vascular Registry 32% of all elective repairs in 2006 were done with endovascular technique (Norkar & Norwegian Society for Vascular Surgery 2006).

3. The policy of treatment must be clear:

An individual approach is recommended, but the threshold of AAA 50-55 mm for elective repair is reported to generally agreed on by in several studies (Brown P.T.MD, David T.Zelt MD, & Boris Sobolev PhD 2003;Lundholm J., Hatlinghus S., Wirsching J, Amundsen S., Staxrud L.E., Gjølberg T., Hafsahl G., Oskarsson W., Krohg-Sørensen, Brekke M., & Myhre H.O. 1999).

4. Provision for diagnosis and treatment must be available:

The screening strategy affects the demand for resources. Bergqvist and co-workers report that screening elderly men has reduced the demand of resources to repair ruptured AAA by 50%, but increased the number of elective repairs by 100-400% (Bergqvist, Bjorck, & Wanhainen 2008). Furthermore, a greater proportion of elective repair is done with endovascular technique than emergency repair. When more patients undergo endovascular repair, the demand for surveillance program after EVAR will increase.

5. The disease must have a detectable latent stage:

AAA involves several years of expansion before the aneurysm reaches the stage, where there is a risk of rupture. Bergqvist and co-workers report that 70% of all screening detected AAA is less than 40 mm, and that 2/3 of all screening detected

AAA never reaches the size of elective repair or rupture (Bergqvist, Bjorck, & Wanhainen 2008).

6. A suitable screening method must be available:

The screening method should show high accuracy, be rapid, inexpensive and safe (Bergqvist, Bjorck, & Wanhainen 2008). In chapter 3 I discussed these criteria with regards to ultrasonography and concluded that the method fulfills the criteria.

7. The screening method must be accepted by the target population:

Ultrasonography has proven to be well accepted in several population-based screening studies, with attendance rates above 75% in most cases (Bergqvist, Bjorck, & Wanhainen 2008).

8. The natural course of the disease must be known:

The natural course of AAA includes both aspects on the aneurysm, as well as the patient carrying the disease. In chapter 1 I presented the most important factors predicting rupture and discussed risk factors for atherosclerosis and AAA. I will not go further into these factors in this section, but summarize that less than 20% of all AAAs eventually ruptures, and that AAAs less than 55 mm have a low risk of rupture.

9. The program must be cost-effective:

This criteria is already discussed in chapters 8 and 9.3

10. The treatment of the disease should favour the prognosis of the patients:

In chapter 1 and 3 I showed that the overall mortality of rupture is high. Elective surgery, in appropriately selected individuals will therefore prevent rupture and improve life expectancy. Furthermore, the long term survival after successful elective repair is only slightly shorter than that of an age-matched general population.

Although screening for AAA seems to fulfill the WHO criteria and fulfill cost-effective criteria, some factors may make screening ineffective. Such factors may be poor attendance rate by elderly people. Elderly people may be skeptical and do not see the value of attending such program. An invitation to screening may also have adverse effect on the quality of life, as discussed in chapter 3. Even though screening for AAA may cause a reduction in aneurysm related mortality, a screening program will also result in some people having surgery for aneurysms that would not have ruptured during their lifetime (Brearly S. & Johnson J.N 2008).

Based on these criteria, AAA seems suitable for a screening program. This is, however, only true for elderly men. The optimal age has not yet been established, but men around 65 years seems to a suitable target group (Bergqvist, Bjorck, & Wanhainen 2008).

The conclusion of this study is that screening 65-year-old men is cost-effective.

10. APPENDIX

Appendix I: Probabilities

Table 7: Table of probabilities included in the model

Probability paramaters included in the model			
Model parameter	**Description**	**Base Case Value**	**Source**
p2Inc	Probability incidentally detection of AAA 30-39 mm	0.051	Henrikson(2005), Assumption
p2_1	Probability of transition from AAA < 30 mm to AAA 30-39 mm	0.0001	Expert opnion
p3Inc	Probability incidentally detection of AAA 40-54 mm	0.08	Henrikson(2005), Assumption
p3_2	Probability of transition from AAA 30-39 mm to 40-54 mm	0.115	Silverstein(2005),Henrikson(2005)
p4Inc	Probability incidentally detection of AAA 55-59 mm	0.11	Henrikson(2005), Assumption
p4_2	Probability of transition from AAA 30-39 mm to AAA 55-59 mm	0.002	Zöllner(1991), Vardulaki(1998)
p4_3	Probability of transition from AAA 40-54 mm to 55-59 mm	0.159	Henrikson(2005)
p5Inc	Probability incidentally detection of AAA > 60 mm	0.125	Henrikson(2005), Assumption
p5_2	Probability of transition from AAA 30-39 mm to AAA > 60 mm (unknown)	0.00001	Expert opinion
p5_3	Probability of transition from AAA 40-54 mm to AAA > 60 mm (unknown)	0.001	Vardulaki(1998)
p5_4	Probability of transition from AAA 55-59 mm to AAA > 60 mm (unknown)	0.17	Vardulaki(1998), Zöllner(1991), Expert opinion
p6_2	Probability of transition from AAA 30-39 mm to AAA > 60 mm	0.00001	Expert opinion
p6_3	Probability of transition from AAA 40-54 mm to AAA > 60 mm (known)	0.001	Vardulaki(1998)
p6_4	Probability of transition from AAA 55-59 mm to AAA > 60 mm (known)	0.17	Vardulaki(1998), Zöllner(1991), Expert opinion
pAneurysmEVAREl	Probability of dying from elective EVAR	0.018	Sakalihasan(2005), Bergqvist(2008), Greenhalgh(2004), Green (2002)
pAneurysmEVAREm	Probability of dying from emergency EVAR	0.4	Dueck(2004), Kantonen(1997), Ashton(2002), Silverstein(2005)
pAneurysmOREl	Probability of dying from elective OR	0.029	Sakalihasan(2005), Bergqvist(2008), Greenhalgh(2004), Green (2002)
pAneurysmOREm	Probability of dying from emergency OR	0.4	Dueck(2004), Kantonen(1997), Ashton(2002), Silverstein(2005)
pAneurysmORPostEVAR	Probability of dying from converted OR	0.18	Sampram(2003), Verzini(2006), Cao(2003)
PAneurysmSecEVAR	Probability of dying from secondary EVAR	0.005	Expert opinion
pDeathRupture	Probability of dying from rupture	0.50	Powell(2001)
pDeathOtherCauses	Probability of dying from other causes	Age specific	See Appendix 4
pEl	Probability of being referred to elective repair	0.84	Henrikson(2005)
pEVAREl	Probability of elective EVAR	0.33	Swedvasc(2005), Norkar(2006)
pEVAREm	Probability of emergency EVAR	0.15	Expert opinion
pIn5_4	Probability of transition from AAA 55-59 mm to AAA > 60 mm, when considered inoperable	0.20	Woodburn(2001), Assumption
pOREl	Probability of elective OR	0.67	Swedvasc(2005), Norkar(2006)
pOREm	Probability of emergency OR	0.85	Expert opinion
pORPostEVAR	Probability of conversion to OR after EVAR	0.02	Greenhalgh(2004), Sampram(2003), Silverstein(2005), Bosch(2002), Hobo(2006)
pRupture2	Probability of rupture of AAA 30-39 mm	0.003	Brown(2003), Vardulaki(1998)
pRupture3	Probability of rupture of AAA 40-54 mm	0.01	Vega(2006), Brown(2003), Henrikson(2005)
pRupture4	Probability of rupture of AAA 55-59 mm	0.065	Green(2002), Zankl(2007), Bergqvist(2008), Wilt(2006)
pRupture5	Probability of rupture of AAA > 60 mm	0.156	Brown(2003), Bergquist(2008), Lederle(2002),
pRuptureInEl4	Probability of rupture of AAA 55-59, considered as inoperable	0.094	Lederle(2002)
pRuptureInEl5	Probability of rupture of AAA > 60 mm (unknown), considered as inoperable	0.15	Lederle(2002)
pRuptureInEl6	Probability of rupture of AAA > 60 mm (known), considered as inoperable	0.15	Lederle(2002)
pSecEVARPostEVAR	Probability of secondary EVAR	0.08	Expert opinion

Appendix II: Costs[28]

Table 8: Pre-operative costs, secondary intervention

Pre-operative costs, secondary intervention (NOK)		
Cost item	**Endovascular repair**	**Source**
CT angio	687	AUH
Co-payment	500	CD
Total pre-operative costs	**1187**	

Table 9: Peri-operative costs

Peri-Operativ costs (NOK)				
Cost item	**Open Repair**	**Endovascular repair**	**Secondary endovascular repair**	**Source**
Personnel				
Number of chief surgeons	2	1	1	AUH
Number of consultant surgeons	1	1	0	AUH
Number of chief radiologists	0	1	1	AUH
Number of consultant radiologists	0	1	0	AUH
Number of chief anaesthetists	1	1	0	AUH
Cost per hour of chief physician	580	580	580	AUH
Cost per hour of consultant physician	461	461	461	AUH
Total cost per hour	*2201*	*2082*	*1160*	
Number of nurses (operation)	2	2	0	AUH
Number of nurses (anaesthesia)	2	2	1	AUH
Number of nurses (radiographs)	0	1	1	AUH
Cost per hour (nurses)	335	335	335	AUH
Total cost per hour (nurses)	*1340*	*1675*	*670*	AUH
Cost per hour operation room	3541	3757	1830	AUH
Mean time in operation room	3	3	1	AUH
Total cost per hour	**10623**	**11271**	**1830**	
Stent graft	3500	83750	6450	AUH
Disposable equipment	4500	4500	4500	AUH
Other equipment	-	10000	13000	AUH
Total cost equipment	**8000**	**98250**	**23950**	
Total peri-operativ costs	**18623**	**109521**	**25780**	

[28] Description of source abbreviation: AUH = Aker University Hospital, CD = Capio Diagnostic

Table 10: Examination costs after discharge from hospital

Examination costs (NOK) after discharge from hospital – First year			
Cost item	**Open repair**	**Endovascular repair**	**Source**
Ultrasound	0	347	AUH
Number of ultrasound	0	3	AUH
X-ray overview	0	102.5	AUH
Number of x-ray overview	0	3	AUH
CT angio	0	687	AUH
Number of CT angio	0	2	AUH
Co-payment	0	500	CD
Number of co-payments	0	3	CD
Out-patient-clinic	700	700	AUH
Number of out-patient-clinic	2	3	AUH
Total cost	**1400**	**6322.5**	

Appendix III: Sensitivity analysis

Table 11: One-way sensitivity analysis on all cost parameters

Model parameter	Description	Base case value	Lower bound	Upper bound
cAneurysmElEVAR	Cost of death from elective EVAR	111755	89404	134106
cAneurysmElOR	Cost of death from elective OR	20857	16686	25028
cAneurysmEmEVAR	Cost of death from emergency EVAR	109521	87617	131425
cAneurysmEmOR	Cost of death from emergency OR	18623	14898	22348
cAneurysmSecEVAR	Cost of death from secondary EVAR	26967	21574	32360
cAneurysmSecOR	Cost of death from secondary OR	19810	15848	23772
cInHospital	Cost of ruptured AAA which does not reach surgery	965	772	1158
cMon2	Cost of monitoring AAA 30-39 mm	1547	1238	1856
cMon3	Cost of monitoring AAA 40-54 mm	1547	1238	1856
cMon4	Cost of monitoring AAA 55-59 mm	3094	2475	3713
cMon5	Cost of monitoring AAA > 60 mm	6188	4950	7426
cPostEVAR	Cost of Post EVAR-programme	950	760	1139
cRupture	Cost of rupture	9953	7962	11944
cScreening_programme	Cost of screening programe	1007	806	1208
cSuccessElEVAR	Cost of successful elective EVAR	228590	182872	274308
cSuccessElOR	Cost of successful elective OR	132770	106216	159324
cSuccessEmEVAR	Cost of successful emergency EVAR	271431	217145	325707
cSuccessEmOR	Cost of successful emergency OR	175611	140489	210733
cSuccessSecEVAR	Cost of successful secondary EVAR	143802	115042	172562
cSuccessSecOR	Cost of successful secondary OR	130536	104429	156643

Table 12: One-way sensitivity analysis on all probability parameters

Model parameter	Description	Base Case Value	Lower bound	Upper bound
p2Inc	Probability incidentally detection of AAA 30-39 mm	0.051	0.051	0.13
p2_1	Probability of transition from AAA < 30 mm to AAA 30-39 mm	0.0001	0,00008	0,00012
p3Inc	Probability incidentally detection of AAA 40-54 mm	0.08	0.051	0.13
p3_2	Probability of transition from AAA 30-39 mm to 40-54 mm	0.115	0.05	0.115
p4Inc	Probability incidentally detection of AAA 55-59 mm	0.11	0.051	0.13
p4_2	Probability of transition from AAA 30-39 mm to AAA 55-59 mm	0.002	0.001	0.004
p4_3	Probability of transition from AAA 40-54 mm to 55-59 mm	0.159	0.1272	0.198
p5Inc	Probability incidentally detection of AAA > 60 mm	0.125	0.051	0.125
p5_2	Probability of transition from AAA 30-39 mm to AAA > 60 mm (unknown)	0.00001	0.000008	0.000012
p5_3	Probability of transition from AAA 40-54 mm to AAA > 60 mm (unknown)	0.001	0.0008	0.0012
p5_4	Probability of transition from AAA 55-59 mm to AAA > 60 mm (unknown)	0.17	0.076	0.17
p6_2	Probability of transition from AAA 30-39 mm to AAA > 60 mm	0.00001	0.000008	0.000012
p6_3	Probability of transition from AAA 40-54 mm to AAA > 60 mm (known)	0.001	0.0008	0.0012
p6_4	Probability of transition from AAA 55-59 mm to AAA > 60 mm (known)	0.17	0.076	0.17
pAneurysmEVAREl	Probability of dying from elective EVAR	0.018	0.012	0.029
pAneurysmEVAREm	Probability of dying from emergency EVAR	0.4	0.3	0.7
pAneurysmOREl	Probability of dying from elective OR	0.029	0.027	0.058
pAneurysmOREm	Probability of dying from emergency OR	0.4	0.3	0.7
pAneurysmORPostEVAR	Probability of dying from converted OR	0.18	0.17	0.24
PAneurysmSecEVAR	Probability of dying from secondary EVAR	0.005	0.004	0.006
pDeathRupture	Probability of dying from rupture	0.50	0.40	0.60
pDeathOtherCauses	Probability of dying from other causes	Age specific		
pEl	Probability of being referred to elective repair	0.84	0.80	0.90
pEVAREl	Probability of elective EVAR	0.33	0.318	0.36
pEVAREm	Probability of emergency EVAR	0.15	0.10	0.20
pIn5_4	Probability of transition from AAA 55-59 mm to AAA > 60 mm, when considered inoperable	0.20	0.16	0.24
pOREl	Probability of elective OR	0.67	0.64	0.682
pOREm	Probability of emergency OR	0.85	0.80	0.90
pORPostEVAR	Probability of conversion to OR after EVAR	0.02	0.016	0.024
pRupture2	Probability of rupture of AAA 30-39 mm	0.003	0.002	0.009
pRupture3	Probability of rupture of AAA 40-54 mm	0.01	0.006	0.027
pRupture4	Probability of rupture of AAA 55-59 mm	0.065	0.05	0.11
pRupture5	Probability of rupture of AAA > 60 mm	0.156	0.1	0.191
pRuptureInEl4	Probability of rupture of AAA 55-59, considered as inoperable	0.094	0.0752	0.1128
pRuptureInEl5	Probability of rupture of AAA > 60 mm (unknown), considered as inoperable	0.15	0.102	0.325
pRuptureInEl6	Probability of rupture of AAA > 60 mm (known), considered as inoperable	0.15	0.102	0.325
pSecEVARPostEVAR	Probability of secondary EVAR	0.08	0.064	0.151

Appendix IV: Background mortality

Table 13: Background mortality, all causes

Age	Mortality rate per 1000 for men in Norway, 2002
65	0,014474
66	0,019075
67	0,021445
68	0,021591
69	0,024721
70	0,025283
71	0,030504
72	0,032119
73	0,038107
74	0,041694
75	0,044814
76	0,05324
77	0,057885
78	0,063012
79	0,074054
80	0,081691
81	0,086522
82	0,111083
83	0,116142
84	0,120478
85	0,150929
86	0,159703
87	0,173087
88	0,204671
89	0,223582
90	0,25132
91	0,267223
92	0,310642
93	0,329744
94	0,327652
95	0,382609
96	0,377273
97	0,564286
98	0,395833
99	0,469388
100	0,460674

Table 14: Background mortality, cardiovascular diseases

Age	Mortality rate per 1000 for men in Norway 2002
65	0,005473454
66	0,006336556
67	0,006512301
68	0,008121492
69	0,008920038
70	0,009283645
71	0,011512195
72	0,012956901
73	0,014580545
74	0,017293178
75	0,019247531
76	0,019457638
77	0,02349646
78	0,02562647
79	0,033588998
80	0,034371132
81	0,037191688
82	0,047898089
83	0,054415073
84	0,05625498
85	0,066471163
86	0,078922934
87	0,071963617
88	0,094388583
89	0,108527132
90	0,117212249
91	0,126652749
92	0,137104506
93	0,145356662
94	0,15530303
95	0,197101449
96	0,172727273
97	0,285714286
98	0,21875
99	0,142857143
100	0,422222222

Appendix V: Validation of the model[29]

Table 15: Remaining life expectancy

Age	Mortality risk	Survival probability population	Conditional survival probability
65	0,014474244	0,985525756	0,985525756
66	0,019074993	0,980925007	0,966726858
67	0,021444547	0,978555453	0,945995839
68	0,021591284	0,978408716	0,925570574
69	0,024721249	0,975278751	0,902689313
70	0,025283118	0,974716882	0,879866513
71	0,030504065	0,969495935	0,853027007
72	0,032119476	0,967880524	0,825628227
73	0,038106642	0,961893358	0,794166307
74	0,041694145	0,958305855	0,761054222
75	0,044814062	0,955185938	0,726948291
76	0,053240386	0,946759614	0,688245283
77	0,057885319	0,942114681	0,648405986
78	0,063011921	0,936988079	0,607548679
79	0,074054483	0,925945517	0,562556976
80	0,081690945	0,918309055	0,516601165
81	0,086521655	0,913478345	0,471903977
82	0,111082803	0,888917197	0,419483561
83	0,116141732	0,883858268	0,370764013
84	0,120478088	0,879521912	0,326095074
85	0,150928641	0,849071359	0,276877988
86	0,159702878	0,840297122	0,232659776
87	0,173087212	0,826912788	0,192389344
88	0,204670775	0,795329225	0,153012868
89	0,223582211	0,776417789	0,118801912
90	0,251319958	0,748680042	0,088944621
91	0,267223382	0,732776618	0,065176538
92	0,310642378	0,689357622	0,044929944
93	0,32974428	0,67025572	0,030114552
94	0,327651515	0,672348485	0,020247473
95	0,382608696	0,617391304	0,012500614
96	0,377272727	0,622727273	0,007784473
97	0,564285714	0,435714286	0,003391806
98	0,395833333	0,604166667	0,002049216
99	0,469387755	0,530612245	0,001087339
100	0,460674157	0,539325843	0,00058643

Remaining life expectancy = 15,929359

[29] Description of validation components: Survival probability population = 1-mortality risk, Conditional survival probability = Survival probability population, current year x Survival probability population, next year

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